4 VISUAL SELECTION AND EVALUATION OF NEUTRAL WORDS IN POST-TRAUMATIC STRESS DISORDER

4.1 SUMMARY

Background: In this study, topographic analysis was used to investigate high-resolution event-related potentials (ERPs) associated with non-target visual stimulus selection and evaluation in post-traumatic stress disorder (PTSD). Previous studies of PTSD have found abnormal discrimination and stimulus evaluation for neutral auditory information, indicated by abnormal target N2/P3 ERPs. Similar abnormality in PTSD was expected for the visual modality.

Task Manipulation: Visual selective attention was required to detect target words in an attended color, given a pseudo-random presentation of red and blue words. The attended words were all candidate targets, as the task required identification of a specific target word in the attended channel. Event-related activity for non-target attended and unattended words is compared for both the scalp potential and scalp current density (SCD).

Results: Attended words elicited greater amplitude in several components: (a) an occipital N120 SCD at 120-140 ms, (b) an occipital N150 ERP and a superior frontal P150 ERP at 140-160 ms, (c) a posterior temporal N180 ERP at 160-180 ms, (d) an occipital P250 SCD at 170-190 ms, and (e) several parietal and frontal components, including a P350 SCD at 340-355 ms, a P400 ERP at 385-415 ms, and a P450 SCD at 410-470 ms. Several group differences were apparent in components arising after 250 ms. The unattended words elicited greater amplitude in an occipital P250 ERP at 235-260 ms, which was related to a posterior temporal ND250 ERP at 265-290 ms that was larger in controls than PTSD patients. The ND250 amplitude was linearly related

to both trait anxiety and depression; it became larger with increasing trait anxiety, but smaller with increasing depression. For patients, there was a negative relationship between ND250 latency and CAPS criterion C; it arose earlier as symptoms of avoidance and withdrawal increased. For the P400 ERP and the P450 SCD, there were attention effects in controls, but not PTSD patients. These attention effects were related to the PD450 ERP/SCD over frontal regions at 440-480 ms, which were also larger for controls than PTSD patients. The PD450 ERP amplitude was negatively related to trait anxiety and depression; as these symptoms increased, the amplitude of the PD450 ERP decreased. Also, the PD450 ERP amplitude was negatively related to target reaction time; with decreases in PD450 amplitude, target reaction time increased.

Conclusions: The scalp electric components suggest that visual discrimination of attended from unattended word features occur in primary and secondary visual systems within 250 ms. There were no clear deficits in this activity for PTSD patients, consistent with some previous findings of normal auditory N1 and P2 ERP components for neutral stimuli in PTSD. Later components in parietal and frontal regions indicate further evaluation of attended stimuli between 250-600 ms. This evaluation processing most likely comprises a comparison of the attended common word against the target word held in working memory. These components indicate abnormal stimulus evaluation processes in PTSD patients. The findings of this study provide new insights into the functional topography of attention and evaluation processes for non-target visual events.

4.2 Selective Attention in Post-traumatic Stress Disorder

A central issue for trauma victims is the process of integrating traumatic experiences with neutral, pre-trauma cognition (Horowitz, 1986). PTSD sufferers do not fully accomplish this integration; they suffer from dissociative states, including oscillations between traumatic intrusion and avoidance (Horowitz, 1986). This failure to process traumatic experience was first identified in the late 19th and early 20th centuries. Janet, a pioneer of trauma research, clearly described PTSD as an attachment to traumatic memories that cannot be resolved and replaced by new experiences; PTSD sufferers are not only,

> *unable to integrate traumatic memories, they seem to have lost their capacity to assimilate new experiences as well. It is . . . as if their personality, which definitely stopped at a certain point, cannot enlarge any more by the addition or assimilation of new elements* (Janet, 1911, cited in van der Kolk et al., 1994, p. 532).

These early insights are now consolidated into the psychological proposition that activation of a threat schema competes for cognitive resources that would otherwise process neutral information (Lang, 1978, 1985; Chemtob, Roitblat, Hamada, Carlson & Twentyman, 1988; Foa, Steketee & Olasov-Rothbaum, 1989). A threat schema is like a play script that comprises all of the sensory-motor, emotional and visceral, and cognitive appraisal processes activated by real or perceived threat or danger (Lang, 1978, 1985). It is arguable that threat schema are often, if not always, active in PTSD. Threat arises not merely from the external stimulus environment, but mostly from disturbing traumatic memories that are always present in PTSD, whether implicit or explicit (McNally, 1997). Any external or internal cues that activate these sensitive memories are avoided, and this avoidance behavior requires vigilance – this vigilance or attention to threat is a background or tonic state of hyperarousal and increased

distractibility. Thus, the potential for threatening distraction in PTSD is always present and, to the extent that it is controllable or perceived to be so, it promotes vigilant avoidance behavior. This avoidance and hypervigilance, in turn, maintain the centrality of the trauma in consciousness and thereby interrupt attention and memory for neutral, non-traumatic information (Chemtob et al., 1988; Foa et al., 1989; Cassiday, McNally & Zeitlin, 1992; McNally, 1997). PTSD patients often report that intrusions escape their conscious control, so they exert more conscious effort to avoid intrusions. This heightened vigilance for trauma cues interrupts the development of effective cognitive structures for processing neutral information (Cassiday et al., 1992; McNally, 1997).

4.2.1 Neuropsychology of Hypervigilance

Susceptibility to traumatic intrusions and poor concentration for neutral information in PTSD may involve not only threat appraisal and hypervigilance, but fundamental abnormality of neural processes involved in selective attention and stimulus evaluation. Substantial research findings support the hypothesis that hyperarousal and distractibility in PTSD arise from neuropathology. Firstly, it is proposed that abnormalities of catecholamine neurotransmission, especially noradrenalin, can impair stimulus discrimination and attention in PTSD (Kolb, 1987; see also Clark, Geffen & Geffen, 1987). Secondly, medial temporal structures, such as the hippocampus, are implicated in anxiety, hypervigilance and impaired episodic memory in PTSD (Gray, 1982; Kolb, 1987; Everly, 1989, 1993; Eichenbaum & Otto, 1993; Bremner et al., 1995, 1997; Gurvitis et al., 1996; McNally, 1997; Nadel & Jacobs, 1996, 1998; Rugg, 1998; Strange et al., 1999; Anagnostaras, Graske, & Fanselow, 1999; Brown, Rush, & McEwen, 1999; McEwen, 1999).

Several neuropsychological studies of PTSD have demonstrated impaired attention and memory processes for neutral stimulus information (Everly & Horton, 1989; Gil et al., 1990; Uddo et al., 1993; Bremner et al., 1993; Yehuda et al., 1995;

Anagnostaras et al., 1999). Abnormal function of the septo-hippocampal system is preferred as an explanation for poor performance in these tasks. The hippocampus and parahippocampal regions play an important role in episodic memory processes, including detection of contextual novelty and, thereby, further evaluation of stimulus meaning (Eichenbaum & Otto, 1993; Rugg, 1998; Strange et al., 1999). Anatomical and neurotransmitter abnormalities in septo-hippocampal circuits will produce abnormal contextual novelty detection and episodic memory. Gray (1982) proposes that noradrenergic hyperactivity in the hippocampus stimulates excessive novelty detection and thereby disrupts coherent evaluation of stimulus information. Several reports indicate that chronic PTSD patients have sustained atrophy of hippocampal structures, caused by excessive activation and glucocorticoid toxicity (Bremner et al., 1995, 1997; Gurvitis et al., 1996; McEwen, 1999; see also Brown et al., 1999). Moreover, these PTSD patients with compromised hippocampal structures show signs of poor episodic memory functioning (Gurvitis et al., 1996; McNally, 1997).

The novelty detection functions of the septo-hippocampal area play an important role in behavioral inhibition, anxiety, and stress responses (Gray, 1982). When an unexpected event occurs, ongoing action plans are halted until further evaluation of the novel event can determine appropriate actions to adapt to the new circumstances. When this behavioral inhibition and cognitive uncertainty frequently arises from abnormal noradrenergic hyperactivity, it can generate neurotic anxiety. That is, excessive novelty detection generates visceral stress responses that are unwarranted and it requires greater effort to reappraise otherwise common events. In time, meta-cognitive processes may identify this persistent novelty detection as a source of error that requires corrective appraisal. Unless these executive processes are associated with neural processes that physically intervene to correct the anomalies of novelty detection, the novelty detection will continue. Persistent, erroneous novelty detection increases uncertainty about the

regularity of otherwise common events and increases stress responses, including a perceived decrease in the capacity to adapt to an increase in the frequency of changing circumstances (Gray, 1982). Thus, abnormality of the novelty detection and stimulus evaluation processes associated with septo-hippocampal function can explain distractibility and associated hyperarousal and anxiety in PTSD.

4.2.2 Neuroimaging of Hypervigilance

Several electrophysiological studies have provided initial clues into the component processes of impaired cognition in PTSD, including sensitive measures of attention biases in PTSD. For instance, during a pictorial target detection task, war veterans with PTSD were distracted by rare combat images, indicated by larger N1 and P3 and a later P3 for combat images (Attias, Bleich & Gilat, 1996; Attias, Bleich, Furman & Zinger, 1996). Furthermore, this increased attention to traumatic images was associated with poor responses to neutral target stimuli (Attias, Bleich, Furman & Zinger, 1996). Moreover, ERP research has also demonstrated abnormal novel stimulus discrimination and evaluation for neutral stimuli, in the absence of any traumatic stimuli (McFarlane et al., 1993; Charles et al., 1995; Metzger et al., 1997; Kimble et al., 2000; Galletly et al., 2001; Felmingham et al., 2002). These difficulties were indicated by abnormal N2/P3 and late slow-wave ERPs, which have been shown to be sensitive to catecholamine neurotransmission (see McFarlane et al., 1993; Metzger et al., 1997). These findings, in particular, could be an indication of the hippocampal dysfunction outlined above, as some evidence indicates that frontal and hippocampal functions contribute to endogenous ERPs, such as the P3 (see McFarlane et al., 1993; Knight, 1996).

4.3 The Present Study

Previous ERP studies of neutral information processing in PTSD have employed elementary auditory stimuli. This study investigates ERP components of visual selective attention and evaluation processes for linguistic stimuli, for which impairments in PTSD have been reported in several neuropsychology studies (Everly & Horton, 1989; Bremner et al., 1993; Gil et al., 1990; Uddo et al., 1993; Yehuda et al., 1995). However, these studies only provide indications of gross information processing impairment in PTSD. This study employs methods of cognitive neuroscience to delineate whether impaired cognition is evident in early stages of visual stimulus discrimination and/or later aspects of stimulus encoding and evaluation. The use of linguistic stimuli provides greater opportunity for encoding and evaluation processing. Furthermore, previous ERP studies of neutral information processing in PTSD have concentrated on later endogenous ERP components for novel stimuli, particularly the target N2/P3 complex. These endogenous ERP variations indicate abnormality of controlled stimulus processing. This involves several cognitive processes, including: (a) early selection and evaluation of attended stimuli, (b) working memory storage and processing, and possibly (c) the preparation, selection and/or execution of appropriate behavioral responses (e.g., Magliero, Bashore, Coles, & Donchin, 1984; Donchin & Coles, 1988; Leuthold & Sommer, 1998; Pritchard, Houlihan, & Robinson, 1999). The current study investigates the high-resolution ERP topography for specific components of visual stimulus discrimination and evaluation.

The study explores selective attention for red and blue words in a target detection task, but note that the ERP activity is not specific to the red or blue color. Previous studies of selective attention to color have investigated checkerboards and geometric shapes, which have found no attention preference for any particular color (Anllo-Vento, Luck, & Hillyard, 1998; Valdes-Sosa, Bobes, Rodriguez, & Pinilla, 1998; Wijers,

Mulder, Okita, & Mulder, 1989; Wijers, Mulder, Okita, Mulder, & Scheffers, 1989; Wijers, Otten, Feenstra, Mulder, & Mulder, 1989). On this basis, given counterbalancing of attention to red or blue words, ERPs in this study were averaged across word color, according to attention condition alone, so there is no confound between attention and color.

The task was designed to evaluate ERP measures of several processing stages. ERPs related to the attended vs. unattended non-target words were examined to determine the timing and topography of event-related brain activity during (a) stimulus selection and (b) subsequent stimulus evaluation. The selection stage differentiates stimuli based on color and the evaluation stage includes a comparison of attended words with a memorized target representation.

Recent developments in our understanding of the complex relationships between sensory-motor systems and executive attention and memory systems call into question whether early sensory/perceptual processes are entirely encapsulated and immune from executive modulation (e.g., Moscovitch, 1992; Desimone & Duncan, 1995; Foxe & Simpson, 2002). Furthermore, recent neuroimaging research and theory poses important questions about whether it is possible to clearly differentiate or isolate discrete stages of information processing (e.g., Foxe & Simpson, 2002). For example, given a series of ERP components that indicate the development of cognitive activity over milliseconds, it has been common to ascribe to each ERP component a particular cognitive process in a series of hierarchically dependent processes. This may apply to exogenous ERP components (although see Foxe & Simpson, 2002), but not so well to endogenous components. More importantly, executive processes may exert tonic modulations of sensory processes and therefore would not exhibit high frequency event-related behavior and would not appear explicitly in the ERP component structure. Rather, the influence of these executive processes appears as modulations of the sensory

ERP components. This can be the case with attention ERPs. Control of the attention allocation is presumed to be frontal and parietal systems and the effects of attention are measured by variations in amplitude or latency of ERP components related to sensory and perceptual processing. With these caveats in mind, this study attempts to isolate and evaluate putative component processes of attention and evaluation cognition, with regard to a sequence of processing stages that begin with visual stimulus processing.

4.3.1 Visual Color Processing Systems

The initial visual detection and feature processing occurs in the visual pathways within 30-120 ms of stimulus onset. The striate cortex receives visual input, via the optic chiasm and the lateral geniculate nucleus of the thalamus, within approximately 40-80 ms of visual stimulus onset and transduction in the retina (Clarke, Halgren, Scarabin, & Chauvel, 1995; Shapley, 1995; Nowak & Bullier, 1997; Lamme, Super, & Spekreijse, 1998; Martinez et al., 1999). The anatomy and physiology of the visual cortex provides insight into how it processes and organizes various visual features, such as location (depth), movement, color, shape, and texture. The striate cortex has not only a vertical laminar structure with different input/output connections, but the cortical sheet is organized into columns, defined by ocular dominance and preferential responses to particular stimulus features, such as orientation, color, contrast and spatial frequency (Van Essen & Deyoe, 1995; Mountcastle, 1997). These preferential responses implement a categorical differentiation of the visual array, which begin as elementary dot/color receptive fields in the retina and lead to larger receptive fields in the visual cortex that represent higher-order visual features and objects. The cortex achieves this categorical differentiation partly through a process of lateral inhibition, whereby columns with receptive fields for particular features inhibit nearby columns with similar, but different receptive fields. This cortical discrimination processing occurs in local cortical areas and multiple thalamo-cortical and cortico-cortical feed-forward and

feedback circuits (see Felleman & Van Essen, 1991; Van Essen & Deyoe, 1995; Callaway, 1998; Lamme et al., 1998; see also Nowak & Bullier, 1997; Pollen, 1999; Koch & Poggio, 1999; Rao, Zhou, Zhou, Fan & Chen, 2003).

The opponent-process theory of color vision describes the competitive activation of the retina and early visual pathways among cells that preferentially respond to elementary color frequencies: red, blue and green (Devalois & Jacobs, 1968). The trichromatic theory of color vision proposes that color discrimination begins in the fovea of the retina, where cone cells have receptive fields that differentiate light frequencies, largely between 300-800 nm (Wald, 1968), within approximately 20-30 ms (Shapley, 1995; Nowak & Bullier, 1997). The cone cells comprise the parvocellular (small cell) projections to the dorsal layers of the lateral geniculate nucleus and then into layers 4A and 4Cβ of the striate cortex (V1; Shapley, 1995; Van Essen & Deyoe, 1995; Callaway, 1998). It has been estimated that these projections arrive in the striate cortex within approximately 10-20 ms, where visual processing of elementary features can be slower, with intralaminar transmissions of the order of 10 ms (Nowak & Bullier, 1997). Further, the parvocellular networks of the striate cortex transmit activity into the ventral inferotemporal cortex within 10-20 ms (Nowak & Bullier, 1997). This includes color processing in the lingual and fusiform gyri (area V4; Damasio, Yamada, Damasio, Corbet, & McKee, 1980; Lueck et al., 1989; Zeki et al., 1991; Allison et al., 1993; Allison, McCarthy, Nobre, Puce, & Belger, 1994; Vaina, 1994; Clark, Fan, & Hillyard, 1995; Sakai et al., 1995; Komatsu, 1998; Lamme et al., 1998; Mesulam, 1998; Chao & Martin, 1999; Martinez et al., 1999).

Note that the latter stages of color processing are approximately 40-60 ms slower than the motion processing system, which includes magnocellular projections to striate cortex, area MT and associated parietal cortex (Nowak & Bullier, 1997). In addition, the timing of activity in the visual cortex is not determined entirely by a serial,

hierarchical processing stream (Nowak & Bullier, 1997; Pollen, 1999). The visual cortex is a complex, highly integrated network of feed-forward and feedback connections that facilitates parallel or concurrent processing of different visual features and the spatio-temporal integration of visual phenomena into coherent percepts (Felleman & Van Essen, 1991; Shapley, 1995; Ts'o & Roe, 1995; Van Essen & Deyoe, 1995; Nowak & Bullier, 1997; Callaway, 1998; Pollen, 1999). Furthermore, we do not fully understand the relationship between processing of visual features in various cortical areas and generation of coherent perceptions, so the timing of cortical processing for visual features may not correspond directly with the timing of visual perception (although see Boucart, 1999; Pollen, 1999). For example, Moutoussis and Zeki (1997) report that perception is faster for color than form and motion, which contradicts the physiological evidence of earlier activity in visual cortex for motion than color and form. However, interpretation of this result must be conditioned by the complexity of decision making processing involved (e.g., see Smid, Jakob & Heinze, 1999, discussed below). Nevertheless, it is important to appreciate that although visual features are processed in different visual cortical regions at different times, the integration or binding of this information into percepts is a complex process that may not be determined by the timing of visual feature processing itself (e.g., Singer, 1995; Pollen, 1999).

Source modeling of visual ERPs indicates visual processing in the primary visual cortex within 60-120 ms of stimulus onset, with color processing in the fusiform area (V4) within 100-150 ms of stimulus onset (Buchner, Weyen, Frackowiak, Romaya & Zecki, 1994; see also Heinze et al., 1994; Hillyard, Mangun, Woldorff & Luck, 1995; Di Russo, Martinez, Sereno, Pitzalis & Hillyard, 2001; Foxe & Simpson, 2002). It has been estimated from ERP source models that transmission from primary visual areas to the extrastriate fusiform area occurs within 20-40 ms (Buchner et al., 1994). These

values are similar to those reported from physiological recordings (see Nowak & Bullier, 1997). ERPs result from volume conduction of activity from large neural assemblies. The spatial scale of measurement and the spatial distortions and timing delays inherent to volume conduction necessitate that precise spatio-temporal localization of ERP sources may not match the figures from physiological studies.

4.3.2 Stimulus Selection

Firstly, the selection stage in the present study requires color discrimination. ERP studies of color based selective attention have identified two or three components in the attention difference waves between 140-350 ms: a small occipital, parietal positive difference (PD at 130 ms), a large occipital selection negativity (SN at 150-350 ms) and an associated frontal selection positivity (FSP at 150-350 ms; Hillyard & Munt, 1984; Aine & Harter, 1986; Wijers et al., 1989a, 1989b, 1989c; Anllo-Vento & Hillyard, 1996; Anllo-Vento et al., 1998; Hillyard & Anllo-Vento, 1998; van der Stelt, Kok, Smulders, Snel, & Gunning, 1998; Valdes-Sosa et al., 1998; Smid et al., 1999).

Smid et al. (1999) investigated the functional significance of these attention components; they demonstrated that the FSP could be an indication of executive attention processes in frontal systems, whereas the SN is related to visual feature processing. They differentiated the functional roles of the SN, FSP and the N2b by manipulation of selective attention to color, shape, or color and shape attributes. Firstly, they found that more difficult feature discriminations delay the onset of all attention components by approximately 50 ms. Secondly, they found that SN and N2b components were equally sensitive to discriminations of color or shape, but the FSP arose approximately 50 ms faster for color than shape (see also Moutoussis & Zeki, 1997). Only when color was difficult to discriminate was the FSP equally responsive to color and shape. Furthermore, only the FSP showed a large and extended sensitivity to detailed shape discriminations, when they were the most relevant attributes for response

selection. Thus, Smid et al. (1999) propose that SN reflects activity in the visual system involved in independent, parallel feature processing, whereas the FSP reflects prefrontal executive activity that integrates stimulus features to facilitate adaptive discrimination and selection-for-action processes.

The timing of these attention components is similar to that demonstrated by physiological measures of the time required for color information to arrive in the extrastriate area (i.e., 140-160 ms). However, it is not clear that the SN is a unitary process, related to stimulus discrimination alone. Although studies demonstrate that the occipital SN is a measure of early visual selection, based on analysis of visual features, the source components of the SN are diverse (Wijers et al., 1989a, 1989b, 1989c; van der Stelt et al., 1998; Smid et al., 1999). Source dipole modelling of the SN indicates activity in several regions (Anllo-Vento et al., 1998). Firstly, the SN at 160 ms is associated with source activity in the ventral visual stream, near the posterior fusiform and lingual gyri (or collateral sulcus, area V4, Anllo-Vento et al., 1998). A later aspect of the SN, at approximately 250 ms, was associated with anterior occipito-temporal activity, indicating higher order stimulus feature or object processing (Anllo-Vento et al., 1998). Anllo-Vento et al. (1998) also identified premotor source activity of the SN at approximately 190 ms, suggesting response preparation. In this regard, note that stimulus selection and evaluation processes may operate in parallel with response preparation, but usually complete before response execution (Wijers et al., 1989; Ilan & Miller, 1999). The location of SN sources in the ventral visual stream is corroborated by neuroimaging studies that clearly demonstrate modulation of the fusiform and lingual cortical areas during attention to color (Damasio et al., 1980; Lueck et al., 1989; Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1990; Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991; Zeki et al., 1991; Petersen, Corbetta, Miezin, & Shulman, 1993; Allison et al., 1994; Vaina, 1994; Sakai et al., 1995; Clark et al., 1997; Komatsu,

1998; Chao & Martin, 1999). Thus, although it is highly likely that the early stages of SN indicate visual discrimination processing, it also appears that the SN is associated with distributed sources that suggest involvement of parallel executive processes.

Like previous studies of color based selective attention, the present study uses colored words, so the stimuli comprise two important feature dimensions, color and form. Early feature analyses of color and form may occur in parallel and the timing of their discrimination, given equal difficulty, may be very similar (Smid et al., 1999; Rao, Zhou, Zhou, Fan, & Chen, 2003). It is most likely, in this study, that attention effects indicate discriminations of color, rather than form. Only color accurately differentiates attended from unattended non-target stimuli in this study. All words are presented in both colors, thereby avoiding any confounds of color and word form in determination of the attended channel. In any case, color discrimination should be easier than discrimination of the form of a target word from other words. Thus, it was expected that color is the preferred attention dimension.

In contrast to previous studies of selective attention to color, which presented letters or shapes, the words of this study also contain linguistic content. It is most likely that visual ERP components at 80-200 ms reflect activity involved in processing elementary stimulus features, such as color, rather than more elaborate linguistic representations. For instance, evidence indicates that it takes approximately 150-200 ms to perceive visual word stimuli as a complete word form, as opposed to a conglomerate of lines with various angles, length, curvature and thickness (Petersen et al., 1993; Allison et al., 1994; Nobre, Allison, & McCarthy, 1994; Halgren, Baudena, Heit, Clarke, & Marinkovic, 1994; Kuriki, Takeuchi, & Hirata, 1998; Schendan, Ganis, & Kutas, 1998; Cohen et al., 2000; Rao et al., 2003). Once a visual stimulus is encoded into a word form, and possibly a linguistic construct, the information it conveys is available for further stimulus evaluation processes.

4.3.3 Stimulus Evaluation

Attended stimuli are candidates for target detection, which involves comparison of attended word attributes against those of a target representation. The target representation is initiated by instruction prior to task commencement and it is maintained by mental rehearsal and repeated target presentations (e.g., Näätänen, 1992). Evaluation of an attended stimulus varies in duration according to its similarity with the target (e.g., Näätänen, 1992). Attended non-target stimuli elicit a medial-frontal N2 (Näätänen & Picton, 1986), while target stimuli elicit a larger medial-frontal N2 and a parietal P3 (Näätänen & Picton, 1986; Näätänen, 1992). This latter ERP complex has been related to extended multimodal stimulus evaluation and response preparation and execution (Magliero et al., 1984; Wijers et al., 1989a, 1989b, 1989c; Pritchard et al., 1999).

In this study, we focus on non-target stimuli, to identify activity related to stimulus evaluation, excluding target response processes. In a similar study, Kellenbach and Michie (1996) report a fronto-central and posterior temporal N2 component, followed by a parietal P3 component. The latter component is interpreted as an indication of stimulus evaluation, similar in nature to the conventional target P3 (Kutas, McCarthy & Donchin, 1977; Duncan-Johnson, 1981; McCarthy & Donchin, 1981; Magliero et al., 1984). The target P3 may be considered to comprise both stimulus evaluation and response related activity (see reviews by Rösler et al., 1986; Johnson, 1988; Näätänen, 1990, 1992). In order to determine that any stimulus is a target, it must be compared with a target representation. Thus, non-target events should elicit a similar degree of stimulus evaluation activity to that of target events, without the associated response execution (see Rösler et al., 1986, esp. figure 4). Target detection for visual word stimuli depends on word form or other linguistic representations. It is assumed that word form perceptions are essential for any further linguistic encoding.

The most elementary target evaluation for visual words involves analysis of letter shapes or Gestalt word perceptions. The encoding of visual word features begins at 90-150 ms, resulting in an orthographic encoding at 150-250 ms, associated with activity in the posterior fusiform and lingual gyri (Petersen et al., 1993; Allison et al., 1994; Nobre et al., 1994; Halgren et al., 1994; Kuriki et al., 1998; Schendan et al., 1998; Cohen et al., 2000; Rao et al., 2003). Recent studies indicate that activity in the posterior fusiform area, related to word form processing, can operate in parallel with activity in nearby cortical regions, related to color perception (Nobre, Allison, & McCarthy, 1998; Smid et al., 1999). Hence, the precise differential measurement of color and form discrimination is very difficult; it can be expected that ERPs alone have a poor capacity to clearly differentiate these processes. Nevertheless, neural activity associated with orthographic processing will appear to some extent in ERPs that arise over occipito-temporal regions at 150-250 ms. Given that this initial orthographic processing is a prerequisite for target detection, ERPs associated with target comparison processes can be expected to arise no earlier than 150-250 ms. Note that this analysis does not preclude the possibility that ERPs in this time frame will measure simultaneous word form and color processing, given that these processes operate in parallel in the ventral visual processing stream. However, it does clearly state that target evaluation processes cannot begin before 150-250 ms.

Further evaluation of attended stimuli may appear in ERP activity after this initial orthographic encoding. The duration of this evaluation processing would depend on whether it operates on the orthographic, phonological or semantic encoding (e.g., Gevins, Cutillo & Smith, 1995).

Further processing of an orthographic stimulus usually translates into phonological and semantic representations (Rumsey et al., 1997; Fujimaki et al., 1999; Pulvermüller, 1999). Phonological representations generate the auditory phonetic

features usually associated with visual linguistic stimuli, which has been related to left temporal activity at 450-500 ms (e.g., Gevins et al., 1995). Semantic representations are more elaborate encoding, which have the advantage of not only more complex representations and associations (e.g., Pulvermüller, 1999), but also more enduring memory (e.g., Buckner & Koutstaal, 1998; Rugg, 1998). Neuroimaging studies demonstrate that semantic encoding of visual words activates a distributed cortical network, including word form areas in lateral temporo-parietal cortex at 200-250 ms (Cohen et al., 2000), anterior fusiform gyrus at 400 ms (Nobre et al., 1994) and lateral prefrontal cortex (Petersen, Fox, & Snyder, 1990; Buckner & Koutstaal, 1998). The proximity of the anterior fusiform gyrus to the entorhinal cortex, hippocampus, and amygdala may facilitate encoding of episodic associations between word perceptions and other multimodal object and emotional perceptions (Nobre et al., 1994). In particular, the hippocampus is important in contextual novelty detection, which can initiate further semantic evaluation, regulated by lateral frontal systems (Eichenbaum & Otto, 1993; Knight, 1996; Tulving, Markowitsch, Craik, Habib, & Houle, 1996; Dolan & Fletcher, 1997; Brewer et al., 1998; Grunwald et al., 1998; Rugg, 1998; Wagner et al., 1998; Opitz, Mecklinger, Friederici, & Cramon, 1999; Saykin et al., 1999; Strange et al., 1999). The frontal cortex contributes executive, strategic processing responsible for coordinating the target detection process and response regulation. Thus, linguistic evaluation is a complex process of information encoding and analysis, which occurs at approximately 200+ ms, involving activity in a distributed neural network.

4.3.4 Hypotheses

4.3.4.1 Visual Selection and Evaluation in PTSD

Kolb (1987) hypothesized that early discrimination processing is impaired in PTSD. This study can provide evidence pertinent to this hypothesis. A previous

finding of sensitivity to stimulus overload (Paige et al., 1990) suggests that PTSD patients have difficulty with early stimulus discrimination for highly salient or intense stimuli. Also, previous ERP studies of traumatic information processing indicate larger N1 ERPs for traumatic stimuli in PTSD, suggesting greater sensory processing and attention for these stimuli (Attias, Bleich & Gilat, 1996; Attias, Bleich, Furman & Zinger, 1996). Furthermore, a report of traumatic visual word processing in PTSD identified a diminished right posterior temporal P1 potential, which was not differentiated for trauma or neutral stimuli, suggesting a general abnormality in discrimination of visual word features in the fusiform area (Kounios et al., 1997). In contrast, most previous ERP studies of neutral information processing indicate no abnormality of early N1 or P2 ERP components (McFarlane et al., 1993; Charles et al., 1995; Metzger et al., 1997; Galletly et al., 2001; cf. Felmingham et al., 2002). Thus, it is unlikely that this study of neutral word processing will identify abnormality of early sensory feature processing in PTSD, indicated by scalp components arising before 200 ms.

Prior studies of neutral information processing have identified an impairment of the discrimination processes associated with the novelty N2 ERP (McFarlane et al., 1993; Charles et al., 1995; Metzger et al., 1997; Galletly et al., 2001; Felmingham et al., 2002). This study should confirm these abnormalities for discrimination in PTSD, at approximately the latency of the N2 component.

Several studies of auditory processing in PTSD indicate that P3 ERP indices of stimulus evaluation are smaller (McFarlane et al., 1993; Charles et al., 1995; Metzger et al., 1997; Felmingham et al., 2002). These processes are independent of stimulus modality, so these deficits can be expected in the visual modality also. However, the P3 ERP component is usually elicited by novel stimuli, indicating several component processes, including stimulus evaluation and response execution. In this study, we

expect to identify and investigate only the stimulus evaluation components of these processes for attended common stimuli. If the previous abnormalities identified in PTSD are related to stimulus evaluation, rather than response execution, we can expect to identify such abnormalities in this study.

4.3.4.2 ERP Indices of Visual Selection and Evaluation

Previous studies of attention to color have identified two main ERP components in the attention difference waves, the selection negativity (SN) and the frontal selection positivity (FSP). These studies indicate selective attention effects in the amplitude of ERP components at 140-160 ms, over occipito-temporal and anterior frontal regions. These studies indicate that attention effects on stimulus discrimination continue until approximately 350 ms.

Stimulus discrimination and evaluation processes have been associated with medial frontal N2 and parietal P3 ERP components, respectively. More elaborate stimulus evaluation evokes larger and longer N2 and P3 components. In this study, the initial orthographic encoding of word stimuli is expected to occur at approximately 200 ms, possibly indicated by occipito-temporal ERP components. This encoding is assumed to be a prerequisite for evaluation of whether a current stimulus is a target word. More elaborate semantic and associative encoding and evaluation of attended stimuli is expected to elicit larger N2 and P3 potentials (e.g., Kellenbach & Michie, 1996). Note that the N2/P3 complex is usually largest for attended target stimuli. Given that all stimuli in this study are non-targets, it was expected that ERP amplitude and duration would be smaller than for the target stimuli (which are compared in a later chapter).

4.4 METHOD

See the general method chapter for details. This chapter focuses on selective attention for colored words in the fixed target task. This involved a pseudo-random presentation of red and blue words, with a counterbalanced design. The attended words were all candidate targets, as the task required identification of a specific target word in the attended channel. Event-related activity for non-target attended and unattended words is compared for both the scalp potential and scalp current density (SCD).

4.5 RESULTS

4.5.1 Task Performance

Patients were both slower to detect targets and detected fewer targets than controls. Patients were not more or less susceptible to false target detection than controls. See the previous task performance chapter for details.

4.5.2 ERP Signal-to-Noise Ratio

The number of EEG trials contributing to averaged ERPs for each condition and each group are summarized in Table 4-1. A two-way ANOVA indicated there were more EEG trials in the averaged ERPs for controls than PTSD patients and for unattended than attended common stimuli (group, $F[1,18] = 5.10$, $p<.05$; attention, $F[1,18] = 113.75$, $p<.001$; group x attention, $F[1,18] = 0.26$, *ns*). All subjects were presented with equal numbers of attended and unattended stimuli, so these differences are solely due to artifact reduction procedures. For all subjects and conditions, no less than 60 trials were averaged to provide a sufficient signal-to-noise ratio for endogenous ERP components arising near or after 80-100 ms (see Table 4-1). Note that very early visual attention effects are difficult to detect, given that they are a fraction of an already small ERP signal, indicating the modulation of the signal source activity. For example,

Anllo-Vento et al. (1998) report ERP averages of over 4,000 EEG trials of checkerboard stimuli at 150-450 ms ISI and that the early C1 component has a magnitude of ±1 μV. Hence, it may be expected that attention effects on the C1, at 60-80 ms, will not be sufficiently resolved in this study, but later, more substantial ERPs should contain sufficient signal to differentiate attention effects.

Table 4-1. Number of EEG trials in averaged ERPs for selective attention conditions.

Fixed Target Task	**Control** [a]				**PTSD** [a]			
Common Stimuli	M	SD	Min	Max	M	SD	Min	Max
Attended	209.80	(41.97)	166	271	153.80	(62.35)	64	264
Unattended	241.90	(51.71)	181	324	183.00	(69.25)	96	314

[a] n = 10.

4.5.3 Event-Related Potential Components

The topographic layouts of group mean ERP waveforms and the attention difference waveforms are given in Figure 4-1, Figure 4-2 and Figure 4-11; all superimposed waveforms are given in Figure 4-3. The waveforms demonstrate a consistent ERP component structure in response to both attended and unattended stimuli, for both groups. The components are further illustrated below, comprising:

- small positive peaks over bilateral occipito-temporal regions at 60-120 ms (P100, see Figure 4-4 & Figure 4-6),
- large negative peaks over bilateral occipito-temporal regions at 100-200 ms (N150), associated with a positive peak over medial frontal regions (P150, see Figure 4-5 & Figure 4-7),
- a large positive peak over occipital and parietal areas at 250 ms (P250, see Figure 4-4, Figure 4-5 & Figure 4-9), and
- a large positive peak over vertex regions at 300-500 ms (P400, see Figure 4-5 & Figure 4-10).

Summary statistics for these components are given in Table 4-2 and the inferential analyses are summarized below (see Table 4-3).

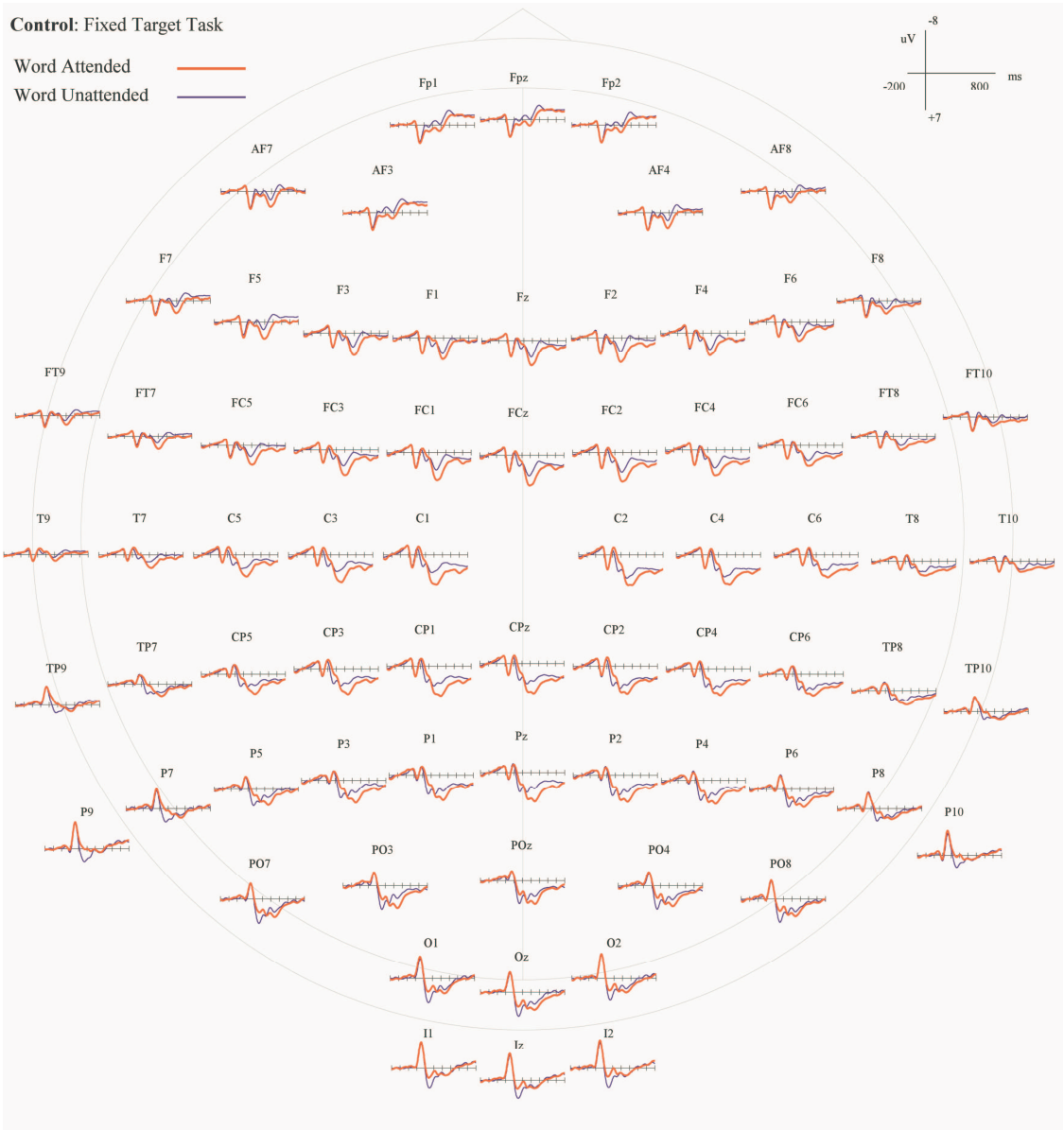

Figure 4-1. ERPs for attended and unattended non-target words in controls (n = 10) at 70 scalp sites (-200 to 800 ms, 100 ms tick marks). The attended words elicit larger positive potentials over parietal, central and frontal regions between 250-600 ms. The unattended words elicit larger negative potentials over occipital, temporal and parietal regions at 200 ms.

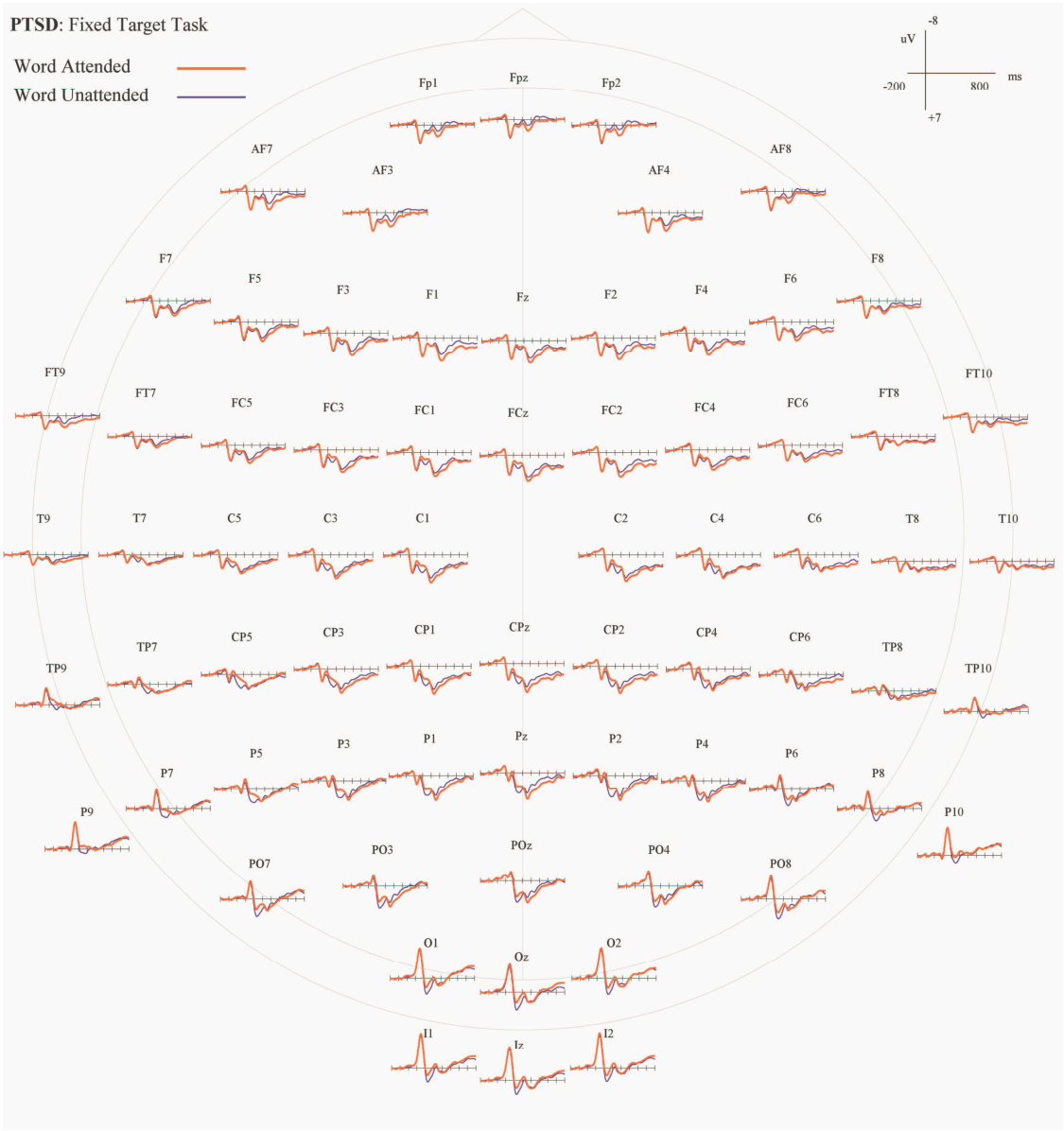

Figure 4-2. ERPs for attended and unattended non-target words in PTSD patients (n = 10) at 70 scalp sites (-200 to 800 ms, 100 ms tick marks). In comparison with controls, there is less difference between the attended and unattended words in the amplitude of the positive potentials over the parietal region.

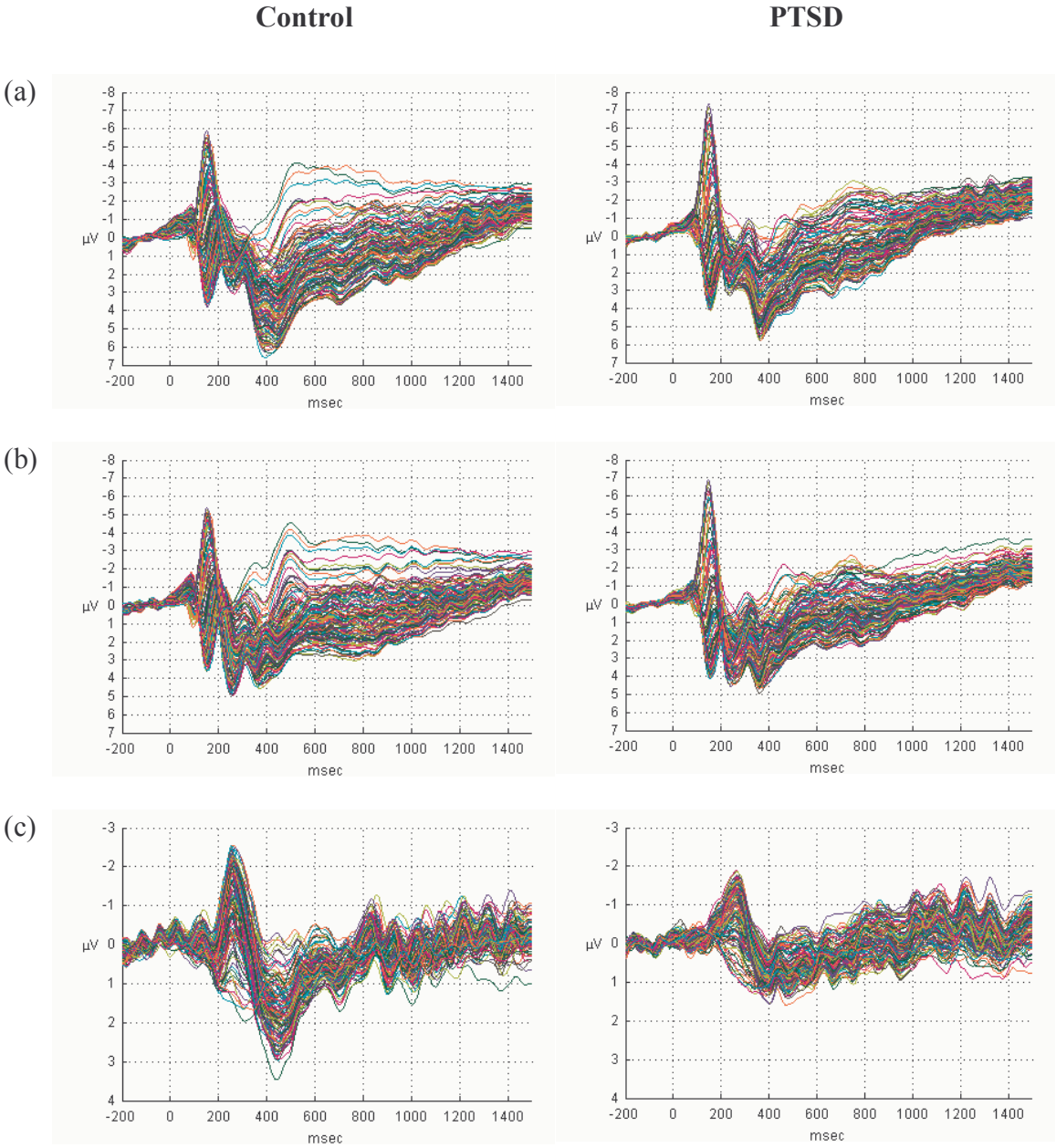

Figure 4-3. ERP waveforms at 124 scalp sites for controls (n=10) and PTSD patients (n=10): (a) attended common words, (b) unattended common words, (c) attended - unattended common words.

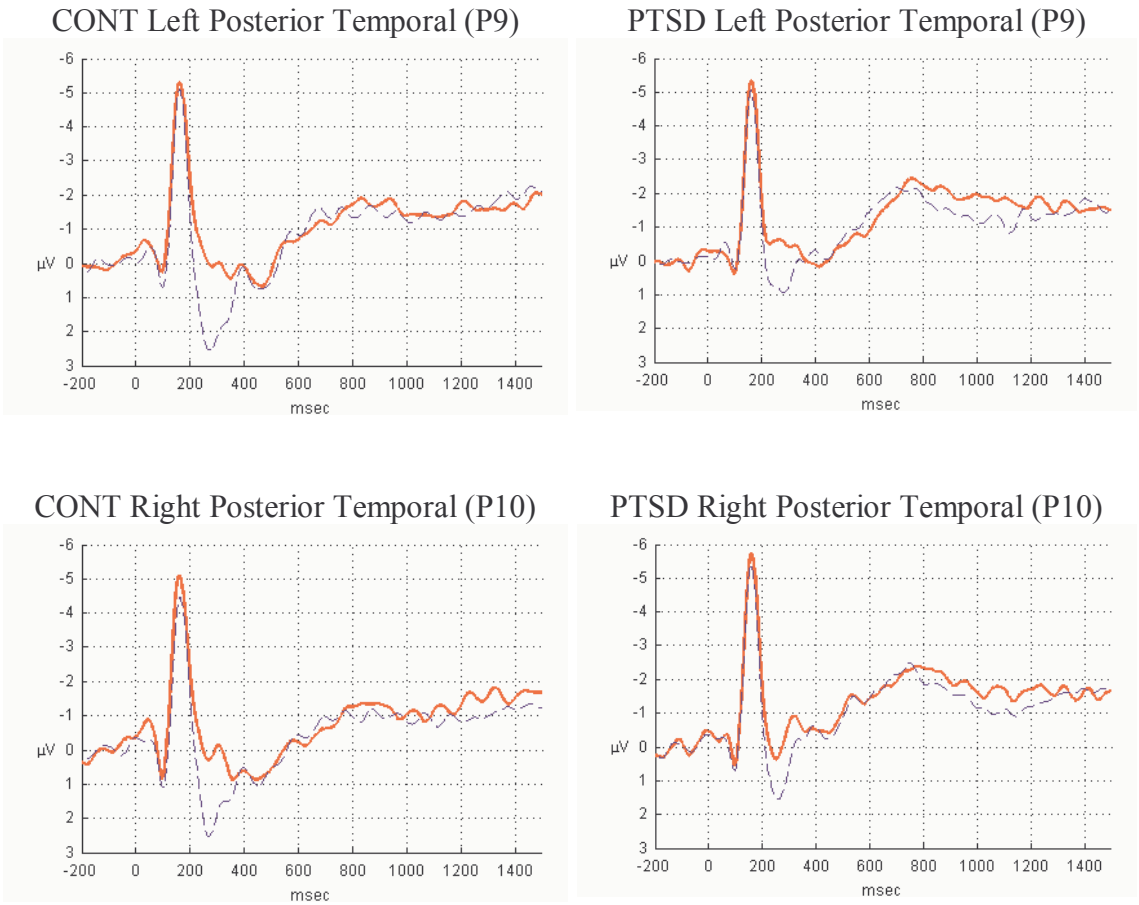

Figure 4-4. ERP waveforms for controls (n = 10) and PTSD patients (n = 10) at left and right posterior temporal sites for both attended (red, solid) and unattended (blue, dash) commons words. Note the small P100 peaks and the larger N150/N180 and P250 peaks. The N150/N180 appeared larger for attended words and the P250 was larger for unattended words, especially for controls. See the topography of these components below.

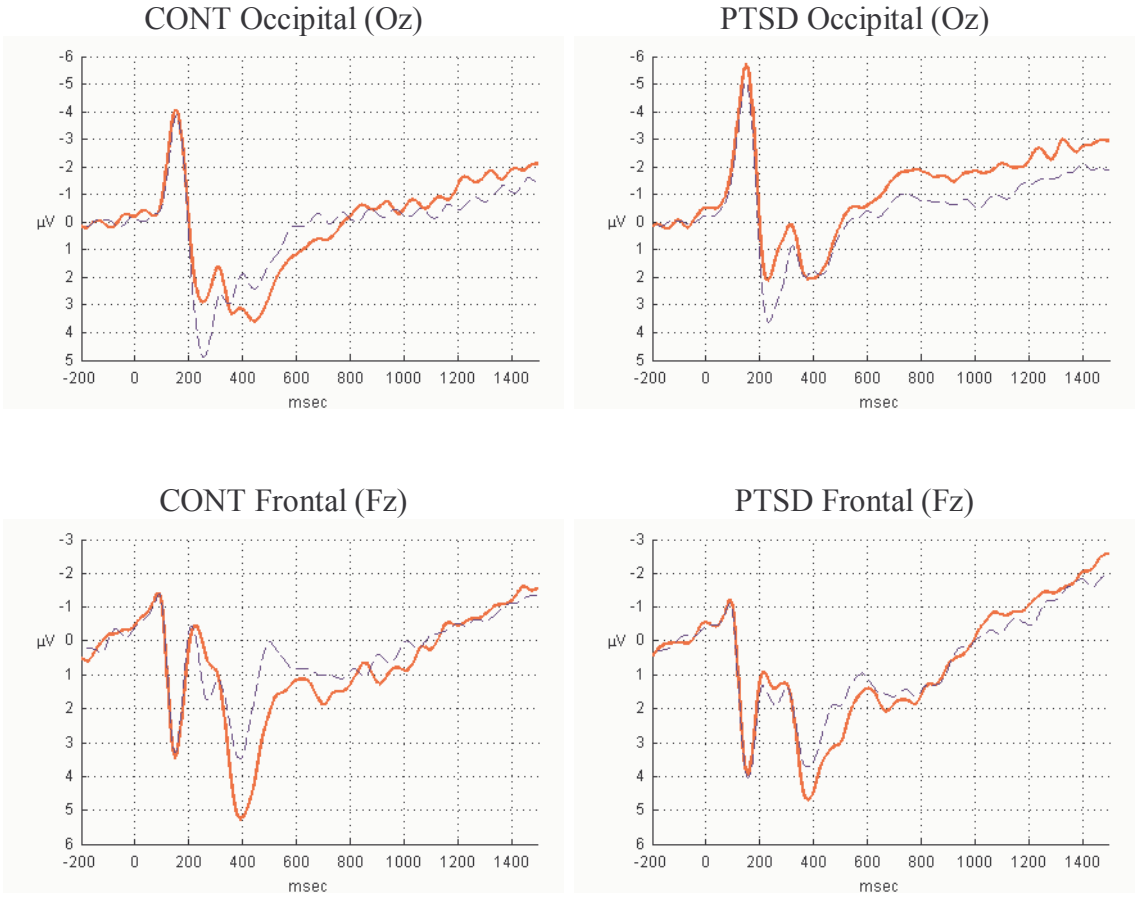

Figure 4-5. ERP waveforms for controls (n = 10) and PTSD patients (n = 10) at occipital and frontal sites for both attended (red, solid) and unattended (blue, dash) common words. Three key features to note: (a) the N150 at Oz and the P150 at Fz, which are larger for patients, (b) the P250 at Oz, which is larger for unattended words and larger for controls, and (c) the P400 at Fz, which is larger for attended words, especially for controls. See the topography of these components below.

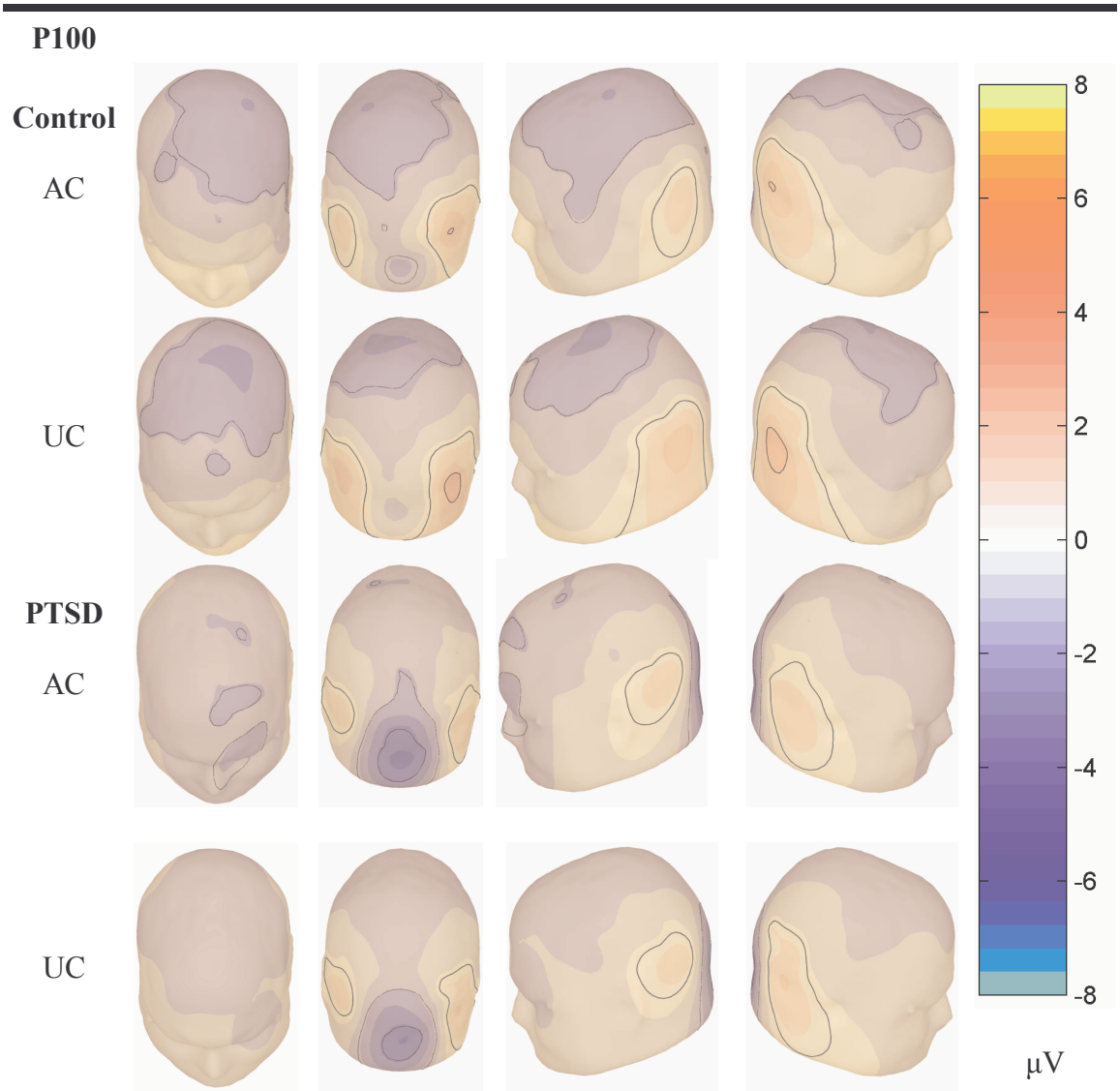

Figure 4-6. P100 ERP topography for controls (n = 10) and PTSD patients (n = 10) at 100 ms for both attended common (AC) and unattended common (UC) words (contours at 1 μV intervals). The P100 comprises small positive peaks at occipito-temporal regions. Note also the negative peaks at occipital regions (which arise into the N150, see below). See Foxe and Simpson (2002), for an example of more detailed analyses at this latency, as this study does not provide very good signal-to-noise to properly cover these early components.

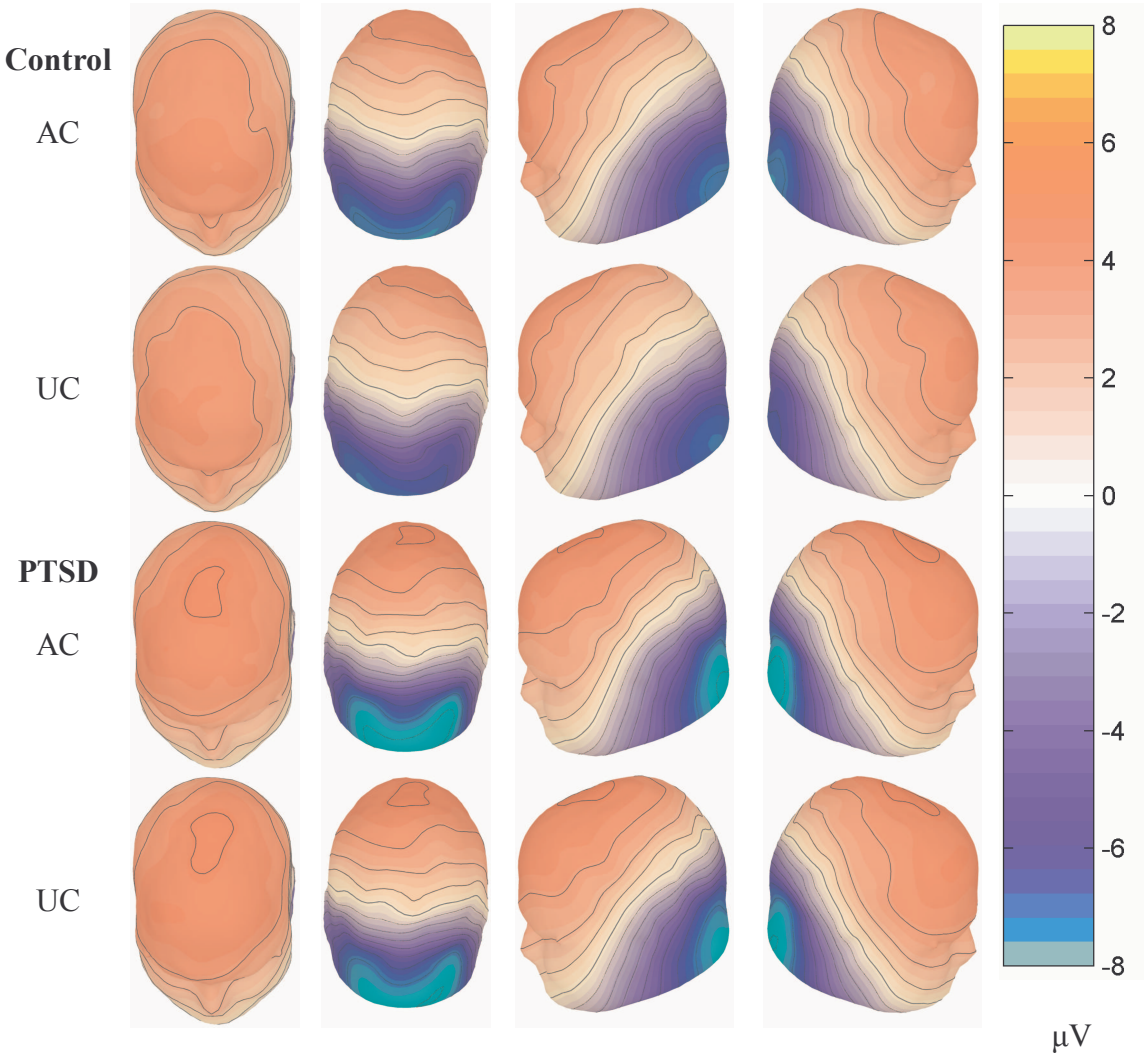

Figure 4-7. ERP topography for N150 (over occipital regions) and P150 (over frontal regions) for controls (n = 10) and PTSD patients (n = 10) at 150 ms for both attended common (AC) and unattended common (UC) words (contours at 1 μV intervals).

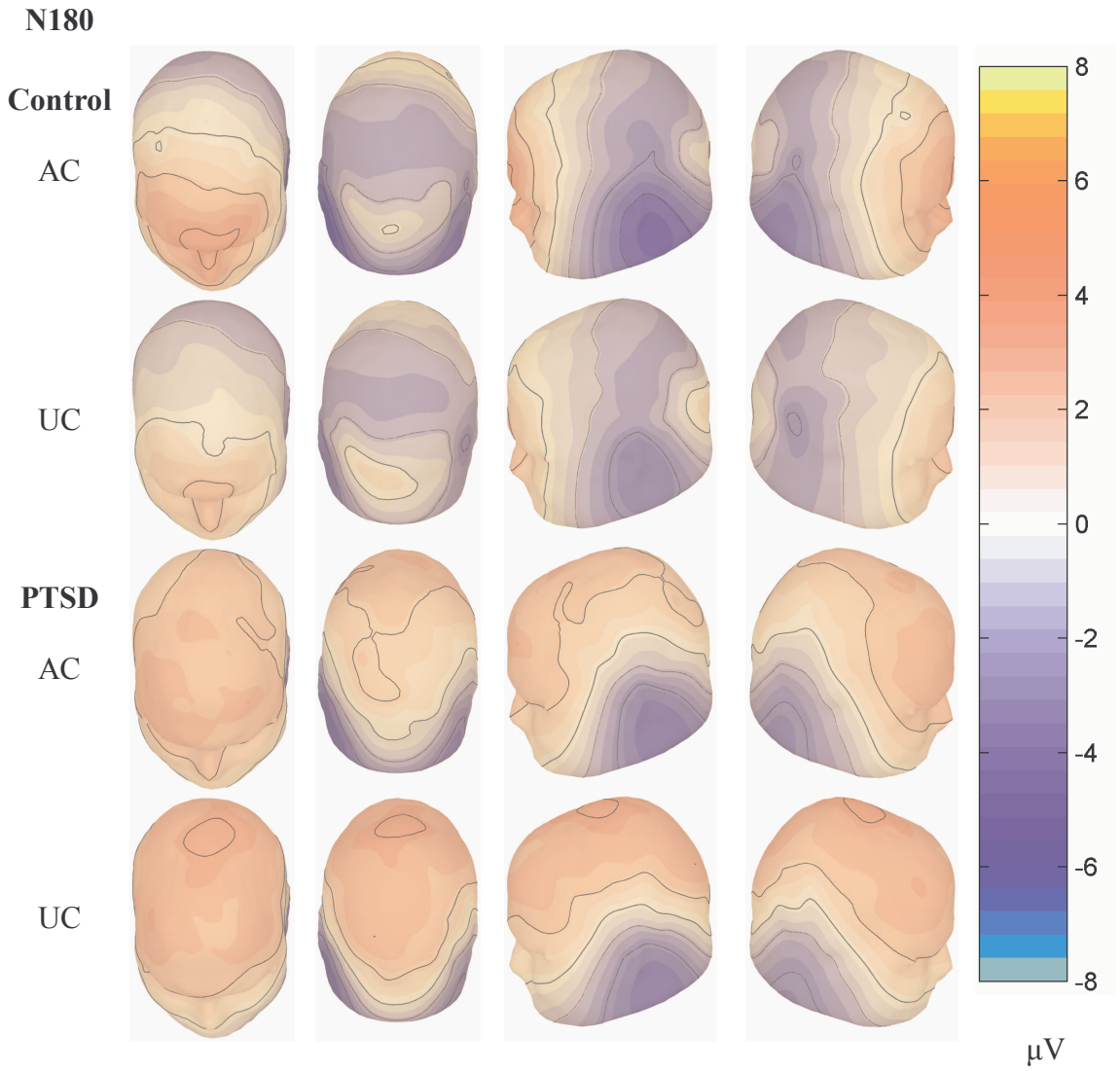

Figure 4-8. ERP topography for N180, over posterior temporal regions, for controls (n = 10) and PTSD patients (n = 10) at 200 ms for both attended common (AC) and unattended common (UC) words (contours at 1 μV intervals).

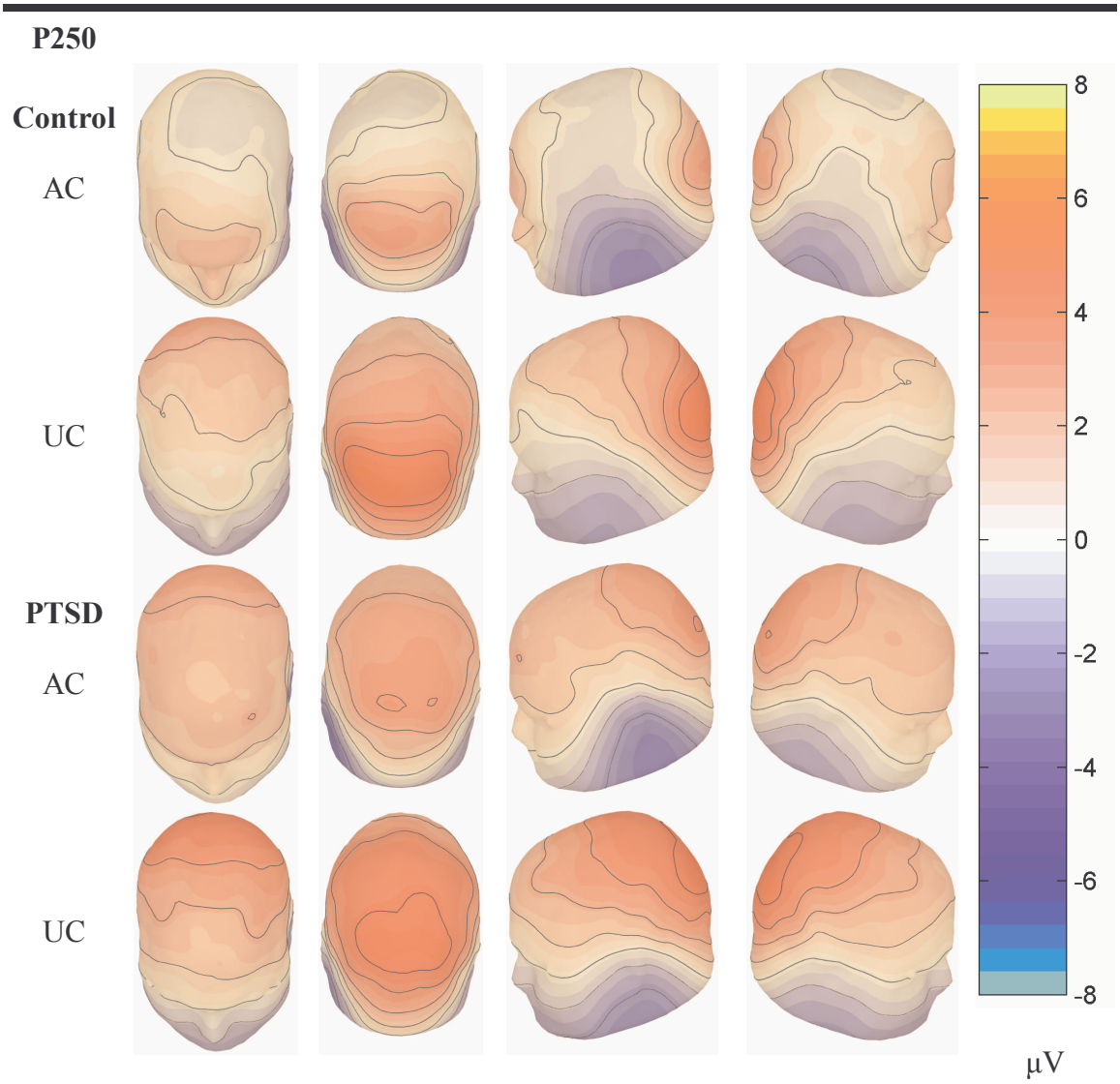

Figure 4-9. P250 ERP topography for controls (n = 10) and PTSD patients (n = 10) at 250 ms for both attended common (AC) and unattended common (UC) words (contours at 1 μV intervals).

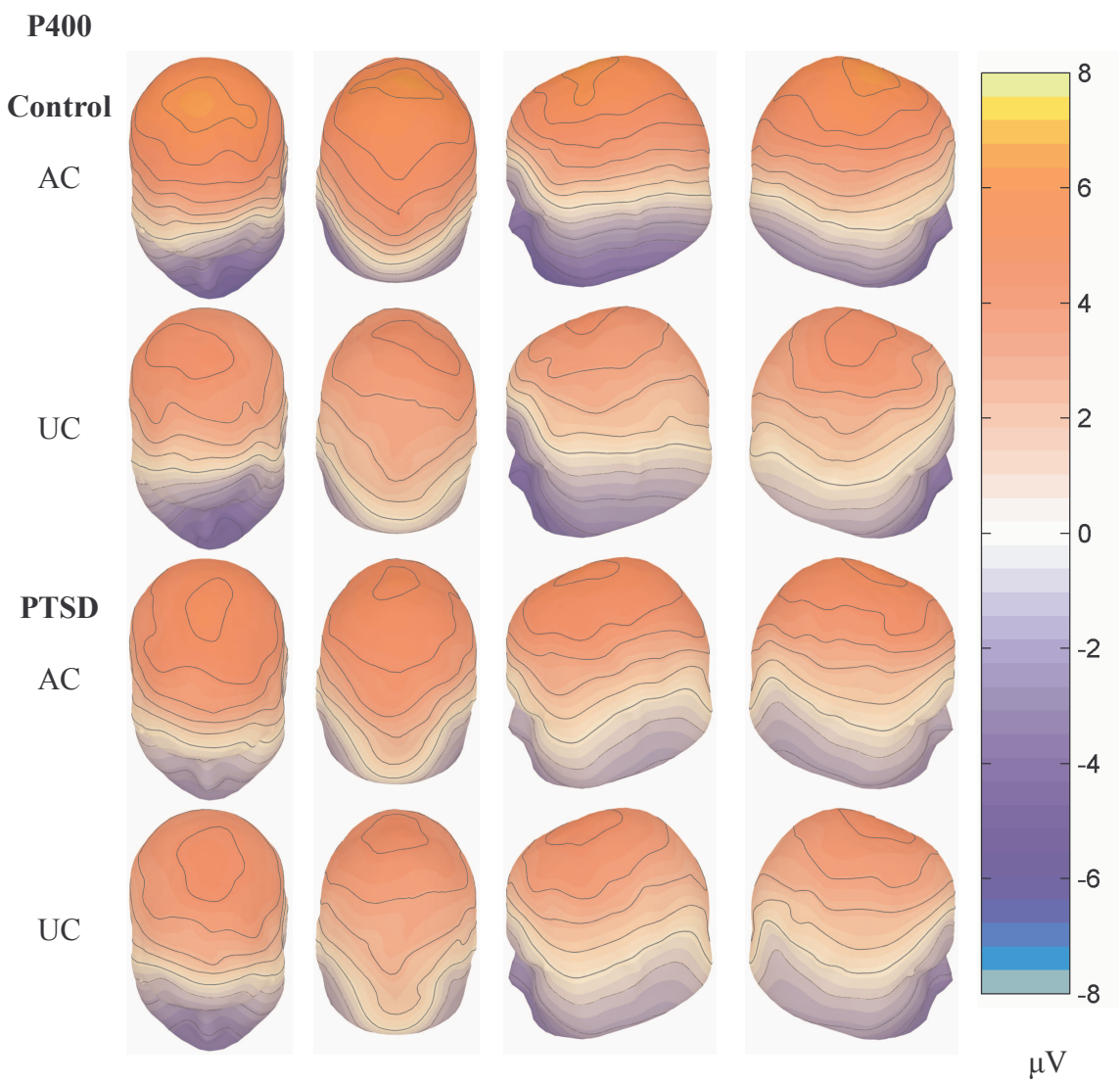

Figure 4-10. P400 ERP topography for controls (n = 10) and PTSD patients (n = 10) at 400 ms for both attended common (AC) and unattended common (UC) words (contours at 1 μV intervals). The P400 was larger for attended than unattended commons, especially for controls. Note that ERP waveforms above indicate more extended processing in controls than PTSD patients.

Table 4-2. ERP Summary Statistics for Attended and Unattended Common Words [a]

			Amplitude (μV)		Latency (ms)	
			CONT	PTSD	CONT	PTSD
P100	Left	AC	1.21 (1.35)	1.89 (1.51)	105.50 (15.80)	98.00 (24.12)
PT		UC	1.24 (1.34)	1.74 (1.52)	95.00 (20.10)	107.00 (16.36)
	Right	AC	1.77 (1.35)	1.53 (1.92)	100.00 (13.28)	109.25 (14.63)
		UC	1.41 (1.52)	1.28 (2.31)	98.25 (11.85)	106.75 (13.02)
N150	Left	AC	-6.59 (4.20)	-8.08 (4.08)	153.50 (14.00)	151.50 (10.75)
OC		UC	-6.04 (4.53)	-7.62 (4.31)	154.50 (13.37)	150.50 (11.71)
	Right	AC	-6.84 (4.00)	-8.26 (2.93)	155.00 (13.99)	145.00 (16.62)
		UC	-6.41 (4.22)	-7.65 (3.33)	157.00 (14.52)	142.25 (18.16)
P150	Left	AC	4.26 (2.51)	4.87 (3.24)	147.00 (16.66)	154.50 (14.13)
SF		UC	3.63 (2.35)	4.89 (3.18)	147.75 (15.65)	156.75 (15.81)
	Right	AC	4.62 (2.48)	4.98 (3.13)	145.75 (19.15)	155.25 (14.07)
		UC	3.94 (2.73)	4.71 (2.66)	149.25 (14.48)	154.75 (17.89)
N180	Left	AC	-6.63 (3.77)	-5.59 (2.66)	176.25 (21.19)	163.00 (9.85)
PT		UC	-6.31 (4.32)	-5.12 (2.61)	172.25 (18.08)	162.00 (10.19)
	Right	AC	-6.81 (3.98)	-6.61 (3.71)	169.25 (23.16)	168.00 (28.16)
		UC	-6.60 (4.15)	-5.87 (4.20)	170.25 (20.43)	171.50 (28.19)
P250	Left	AC	4.29 (3.04)	4.60 (3.81)	243.00 (33.37)	237.50 (31.05)
OC		UC	5.85 (3.74)	5.69 (3.87)	247.25 (20.80)	250.50 (29.67)
	Right	AC	4.23 (2.54)	4.37 (4.04)	248.00 (31.66)	243.00 (28.79)
		UC	5.56 (2.28)	5.22 (4.04)	258.00 (25.46)	257.50 (28.55)
P400	Left	AC	7.72 (4.36)	6.24 (3.32)	411.50 (33.71)	404.50 (50.54)
SF		UC	5.18 (2.90)	5.54 (3.70)	399.75 (35.81)	387.25 (29.82)
	Right	AC	7.99 (2.99)	6.45 (3.26)	407.75 (32.88)	396.00 (54.09)
		UC	5.53 (3.08)	5.25 (3.74)	397.00 (32.95)	387.25 (30.22)

[a] Values are mean (SD); AC = Attended Commons, UC = Unattended Commons; PT = posterior temporal, OC = occipital, SF = superior frontal; CONT, n=10; PTSD, n=10.

Table 4-3. Inferential Statistics for Selective Attention ERP Components [a]

ERP		GP	SA	GPxSA	HS	GPxHS	SAxHS	GPxSAxHS
P100	Amp	0.11	1.71	0.01	0.00	1.15	1.69	0.59
PT	Lat	1.17	0.26	2.72	0.33	0.75	0.08	4.33
N150	Amp	0.69	7.33*	0.01	0.27	0.06	0.01	1.13
OC	Lat	2.08	0.04	3.28	0.62	1.90	0.16	2.16
P150	Amp	0.37	5.41*	2.54	1.91	2.74	0.72	0.36
OC	Lat	1.33	0.74	0.13	0.07	0.16	0.00	1.57
N180	Amp	0.34	6.36*	0.97	0.35	0.12	0.08	0.42
PT	Lat	0.50	0.01	0.81	0.13	2.31	2.73	0.01
P250	Amp	0.00	11.77**	0.45	0.92	0.09	0.97	0.00
OC	Lat	0.03	3.74	0.38	2.28	0.03	0.68	0.23
P400	Amp	0.00	19.87***	3.99†	0.37	0.65	0.30	0.64
SF	Lat	0.50	1.99	0.01	1.91	0.03	1.28	0.80

[a] Values are F[1,18], GP = group, SA = selective attention, HS = hemisphere.

* p<.05, ** p<.01, *** p<.001, *2-tailed*; † p<.05, †† p<.01, ††† p<.001, *1-tailed*.

4.5.3.1 P100 ERP

P100 amplitude was largest over bilateral posterior temporal regions between 60-125 ms (see Figure 4-4, Figure 4-6 & Table 4-2). There were no significant differences in either P100 amplitude or latency (see Table 4-3).

4.5.3.2 N150 ERP

N150 peak amplitude was largest at bilateral occipital regions between 90-200 ms (see Figure 4-4, Figure 4-5, Figure 4-7 & Table 4-2). ANOVA indicated a significant attention effect on N150 amplitude (see Table 4-3). The mean N150 amplitude was larger (more negative) for attended than unattended commons (M = -0.51 μV, SE = 0.19 μV, p<.05).

4.5.3.3 P150 ERP

The P150 was largest over the superior frontal regions between 90-200 ms (see Figure 4-5, Figure 4-7 & Table 4-2). ANOVA indicated a significant attention effect on P150 amplitude (see Table 4-3). The mean P150 amplitude was larger for attended than unattended common words (M = 0.39 μV, SE = 0.17 μV, p<.05).

4.5.3.4 N180 ERP

The N180 peak amplitude was largest over bilateral posterior temporal regions between 150-250 ms (see Figure 4-4, Figure 4-8 & Table 4-2). ANOVA indicated a significant attention effect on N180 amplitude (see Table 4-3). The mean N180 amplitude was larger (more negative) for attended than unattended common words (M = -0.44 μV, SE = 0.17 μV, p<.05).

4.5.3.5 P250 ERP

The P250 peak amplitude was largest over bilateral occipital regions at 190-300 ms (see Figure 4-4, Figure 4-5, Figure 4-9 & Table 4-2). ANOVA indicated a significant attention effect on P250 amplitude (see Table 4-3). The mean P250 amplitude was smaller for attended than unattended common words (M = -1.21 μV, SE = 0.35 μV, p<.01).

4.5.3.6 P400 ERP

P400 peak amplitude was largest over the superior frontal region at 300-500 ms (see Figure 4-5, Figure 4-10 & Table 4-2). ANOVA indicated a significant interaction of group and attention on P400 amplitude (see Table 4-3). The P400 mean amplitude was larger for attended than unattended commons for controls (M = 2.50 μV, SE = 0.55 μV, p<.001), but not for PTSD patients (M = 0.95 μV, SE = 0.55 μV, *ns*).

4.5.3.7 Summary of ERP Findings

Significant differences were found in the following ERP components:

- an occipital N150 and a superior frontal P150 were larger for attended words at 140-160 ms,
- a posterior temporal N180 was larger for attended words at 160-180 ms,
- an occipital P250 was smaller for attended than unattended words at 235-260 ms (which is consistent with previous literature, discussed further below), and
- a superior frontal P400 was larger for attended words at 385-415 ms in controls, but not patients.

4.5.4 ERP Difference Wave Components

The attention difference waves demonstrate two clear components: (a) a negative peak at 250 ms over frontal regions (ND250) and (b) a large positive peak at 450 ms over parietal and frontal regions (PD450; see Figure 4-3 and Figure 4-11 to Figure 4-13). The summary statistics for these components are given in Table 4-4 and the inferential statistics are described below (see Table 4-5).

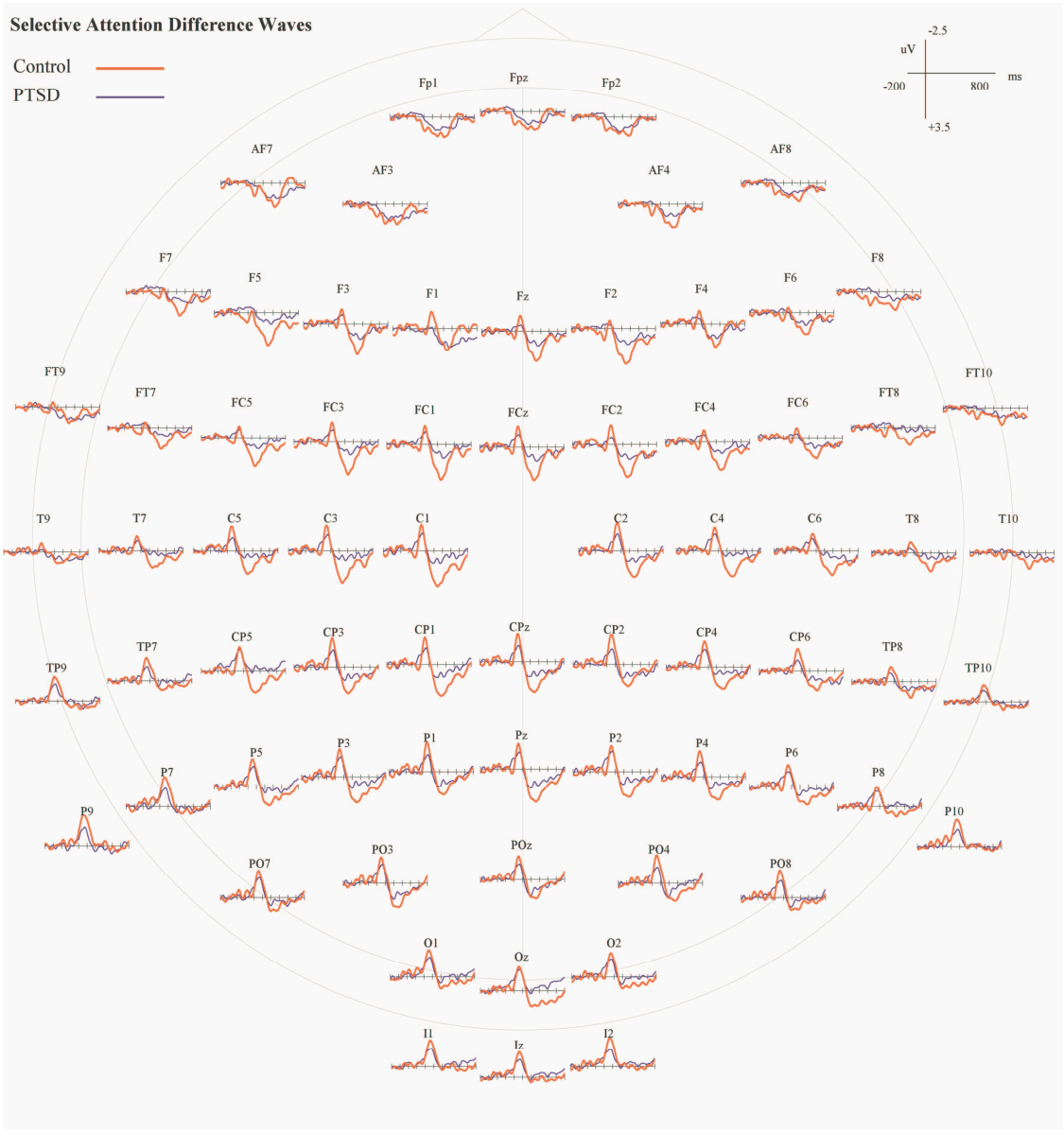

Figure 4-11. ERPs at 70 scalp sites for attention difference waves in controls (n = 10) and PTSD patients (n = 10; -200 to 800 ms, 100 ms tick marks). Note the ND250 over posterior temporal and frontal regions and the PD450 over frontal, central, parietal and occipital regions. The ND250 and the PD450 appear larger for controls than patients. See the topography below.

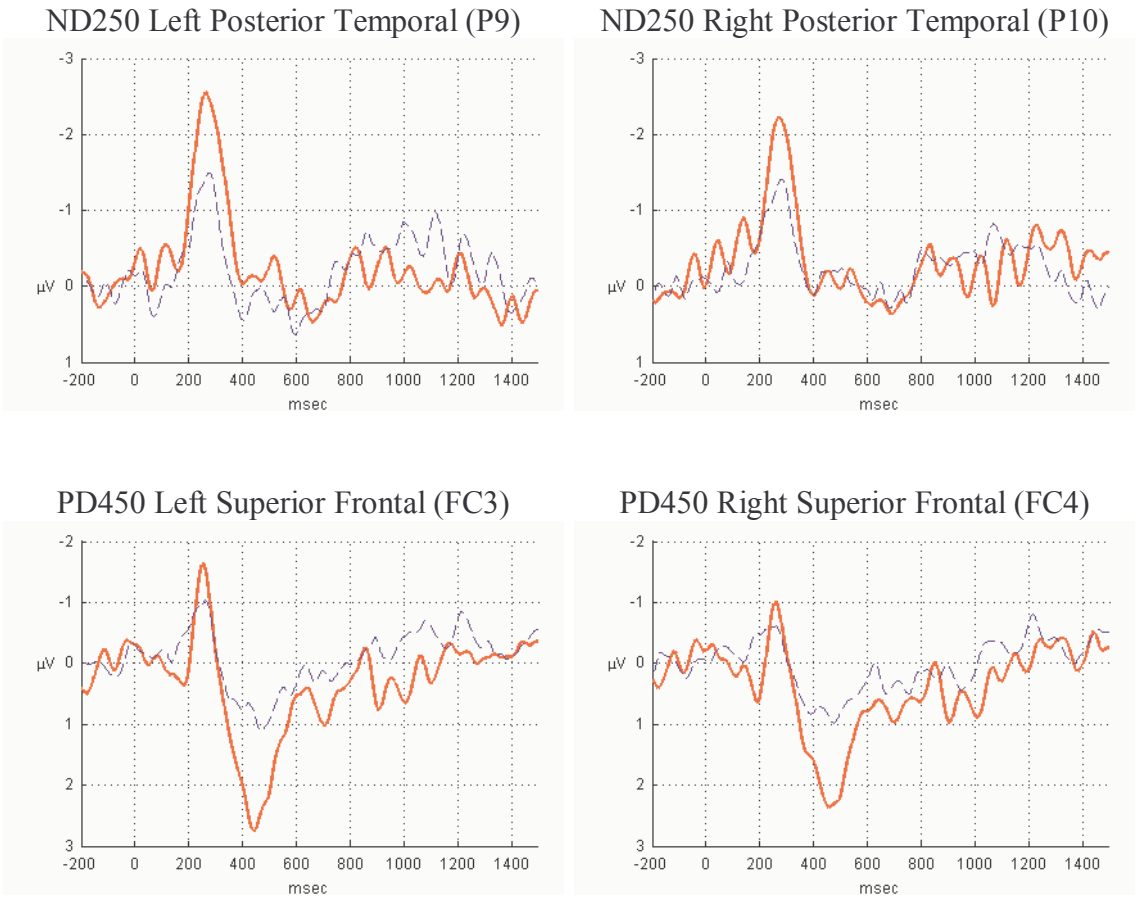

Figure 4-12. ND250 and PD450 ERP attention difference waveforms for controls (n = 10; red, solid) and PTSD patients (n = 10; blue, dash). Note that both the ND250 and the PD450 are larger for controls.

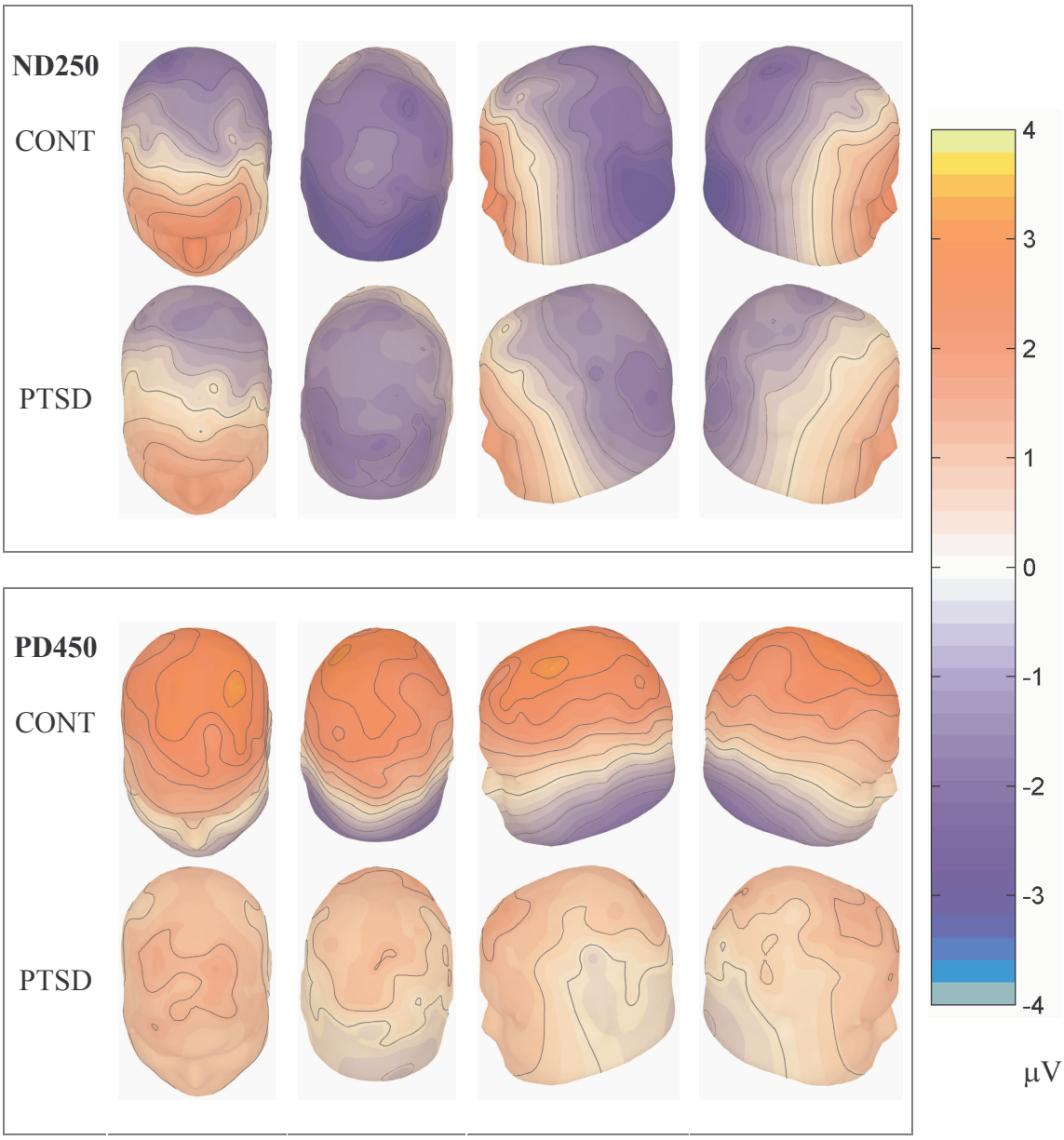

Figure 4-13. ND250 and PD450 ERP topography for controls (n = 10) and PTSD patients (n = 10; contours at 0.5 μV intervals). The ND250 peak, illustrated at 280 ms, is largest over posterior temporal regions and larger for controls than patients. The PD450, illustrated at 450 ms, is largest over superior frontal regions and larger for controls than patients.

Table 4-4. ERP Summary Statistics for Attended - Unattended Common Words [a]

		Amplitude (μV)		Latency (ms)	
		CONT	PTSD	CONT	PTSD
ND250	Left	-3.53 (1.60)	-2.40 (1.02)	282.75 (29.78)	265.75 (28.48)
PT	Right	-3.07 (1.19)	-2.34 (1.16)	280.50 (31.60)	287.50 (30.00)
PD450	Left	4.67 (2.82)	2.20 (1.15)	449.25 (51.72)	452.00 (66.62)
SF	Right	4.44 (1.31)	2.73 (1.23)	444.75 (57.14)	463.50 (65.15)

[a] Values are mean (SD); PT = posterior temporal, SF = superior frontal; CONT, n = 10; PTSD, n = 10.

Table 4-5. Inferential Statistics for Selective Attention ERP Difference Components [a]

ERP		GP	HS	GPxHS
ND250	Amp	3.27 †	1.19	0.69
PT	Lat	0.17	2.92	4.43 *
PD450	Amp	8.74 **	0.17	1.16
SF	Lat	0.23	0.05	0.28

[a] Values are $F[1,18]$, GP = group, HS = hemisphere.

* $p<.05$, ** $p<.01$, *** $p<.001$, *2-tailed*; † $p<.05$, †† $p<.01$, ††† $p<.001$, *1-tailed*.

4.5.4.1 ND250 ERP

The ND250 was a large negative difference peak at 200-300 ms, which was associated with the P250 ERP that was larger for unattended than attended commons (see Figure 4-1, Figure 4-2 & Figure 4-4). ND250 peak amplitude between 180-350 ms was largest over bilateral posterior temporal region (see Figure 4-12, Figure 4-13 & Table 4-4). ANOVA indicated a significant group difference in ND250 mean amplitude and an interaction of group and hemisphere in ND250 mean latency (see Table 4-5). The mean ND250 amplitude was larger for controls than PTSD patients (M = -0.92 μV, SE = 0.51 μV, $p<.05$). The ND250 arose earlier over the left than the right posterior temporal region in PTSD patients (M = -21.75 ms, SE = 8.07 ms, $p<.05$), but not so for controls (M = 2.25 ms, SE = 8.07 ms, *ns*).

Multiple regression analysis indicated a significant linear relationship between ND250 amplitude and both trait anxiety ($\beta = -0.09 \pm 0.04$, $F(17) = -2.17$, $p<.05$) and depression ($\beta = 0.13 \pm 0.05$, $F(17) = 2.47$, $p<.05$). The linear regression equation is: mean(ND250 amplitude) = -0.89 + -0.09(trait anxiety) + 0.13(depression). That is, for each unit increase in trait anxiety (STAI), given constant depression, the mean ND250 amplitude changes by -0.09 μV (i.e., it gets larger). Conversely, for each unit increase in depression (BDI), given constant trait anxiety, the mean ND250 amplitude changes by 0.13 μV (i.e., it gets smaller).

Also, for patients only, there was a significant negative linear relationship between ND250 latency and CAPS criterion C [$r(17) = -.71$; $\beta = -1.93 \pm 0.72$, $F(17) = -2.66$, $p<.05$; $R^2 = 0.51$]. The linear regression equation is: mean(ND250 latency) = 323.06 - 1.93(CAPS C). That is, for each unit increase in CAPS criterion C (avoidance and withdrawal), the mean ND250 latency changes by -1.93 ms (i.e., it decreases).

4.5.4.2 PD450 ERP

A large positive difference peak appeared at 350-550 ms over superior frontal and parietal regions (see Figure 4-11). The PD450 component arose from larger positive potentials at 350-550 ms for attended than unattended commons (see Figure 4-1, Figure 4-2 & Figure 4-5). The PD450 peak was measured between 350-550 ms and it was greatest over superior frontal regions (see Figure 4-12, Figure 4-13 & Table 4-4). ANOVA indicated a significant group difference in ND250 mean amplitude (see Table 4-5). The PD450 mean amplitude was larger for controls than PTSD patients ($M = 2.09$ μV, $SE = 0.71$ μV, $p<.01$).

There was a significant negative linear relationship between PD450 amplitude and trait anxiety [$r(17) = -.44$; $\beta = -0.05 \pm 0.03$, $F(17) = -2.17$, $p<.05$; $R^2 = 0.19$]. The linear regression equation is: mean(PD450 amplitude) = 6.01 - 0.05(trait anxiety). That is, for

each unit increase in trait anxiety (STAI), the mean PD450 peak amplitude changes by -0.05 μV (i.e., it decreases). Similarly, there was a significant negative linear relationship between PD450 amplitude and depression [$r(17) = -.48$; $\beta = -0.07 \pm 0.03$, $F(17) = -2.19$, $p<.05$; $R^2 = 0.23$]. The linear regression equation is: mean(PD450 amplitude) = 4.59 - 0.07(depression). That is, for each unit increase in depression (BDI), the mean PD450 amplitude changes by -0.07 μV (i.e., it decreases).

Also, there was a significant negative linear relationship between PD450 amplitude and target reaction time [$r(17) = -.49$; $\beta = -0.01 \pm 0.005$, $F(17) = -2.13$, $p<.05$; $R^2 = 0.24$]. The linear regression equation is: mean(PD450 amplitude) = 8.81 - 0.01(RT). That is, for each ms increase in target reaction time, the mean PD450 amplitude changes by -0.01 μV (i.e., it tends toward zero).

4.5.4.3 Summary of ERP difference waves

ND250 ERP: The ND250 was a large negative attention difference over bilateral posterior temporal regions between 265-290 ms. The ND250 amplitude was larger in controls than PTSD patients. Also, ND250 arose earlier over the left than the right posterior temporal region in PTSD patients, but not controls. The mean ND250 peak amplitude was linearly related to both trait anxiety and depression; it became larger with increasing trait anxiety, but smaller with increasing depression. For patients, there was a negative relationship between ND250 peak latency and CAPS criterion C; it arose earlier as symptoms of avoidance and withdrawal increased.

PD450 ERP: A large positive attention difference component peaked over medial frontal and central regions at 440-465 ms, where the P400 ERPs were larger and longer for attended than unattended commons. PD450 peak amplitude was larger for controls than PTSD patients. There were no significant differences in PD450 latency. The PD450 peak amplitude was negatively related to trait anxiety and depression; as these

symptoms increased, the amplitude of the PD450 decreased. Also, the PD450 peak amplitude was negatively related to target reaction time; with decreases in PD450 peak amplitude, target reaction time increased.

4.5.5 Scalp Current Density Components

The time series of SCD activity is illustrated at the electrode locations in Figure 4-14 and Figure 4-15, while the overall SCD component structure is clearer in the superimposed waveforms of Figure 4-16. The difference wave components are discussed below. There was similar SCD waveforms for both groups and the following SCD peaks were identified for further analyses:

- early negative peaks at 80-140 ms over the occipital region (N120), associated with positive peaks over bilateral posterior temporal regions (P120, see Figure 4-17 & Figure 4-18),
- a large positive peak arose over the medial parietal area at 150 ms (P150, Figure 4-19, Figure 4-20 & Figure 4-21),
- large negative peaks over occipito-temporal and frontal areas at 180 ms (N180, see Figure 4-22 & Figure 4-23),
- a large positive peak arose at 250 ms over occipital and parietal regions (P250, see Figure 4-24 & Figure 4-25),
- several positive peaks between 350-450 ms over parietal and frontal regions (P350/P450; see Figure 4-26 to Figure 4-30).

Summary statistics for these components are given in Table 4-6 and the inferential analyses are summarized below (see Table 4-7).

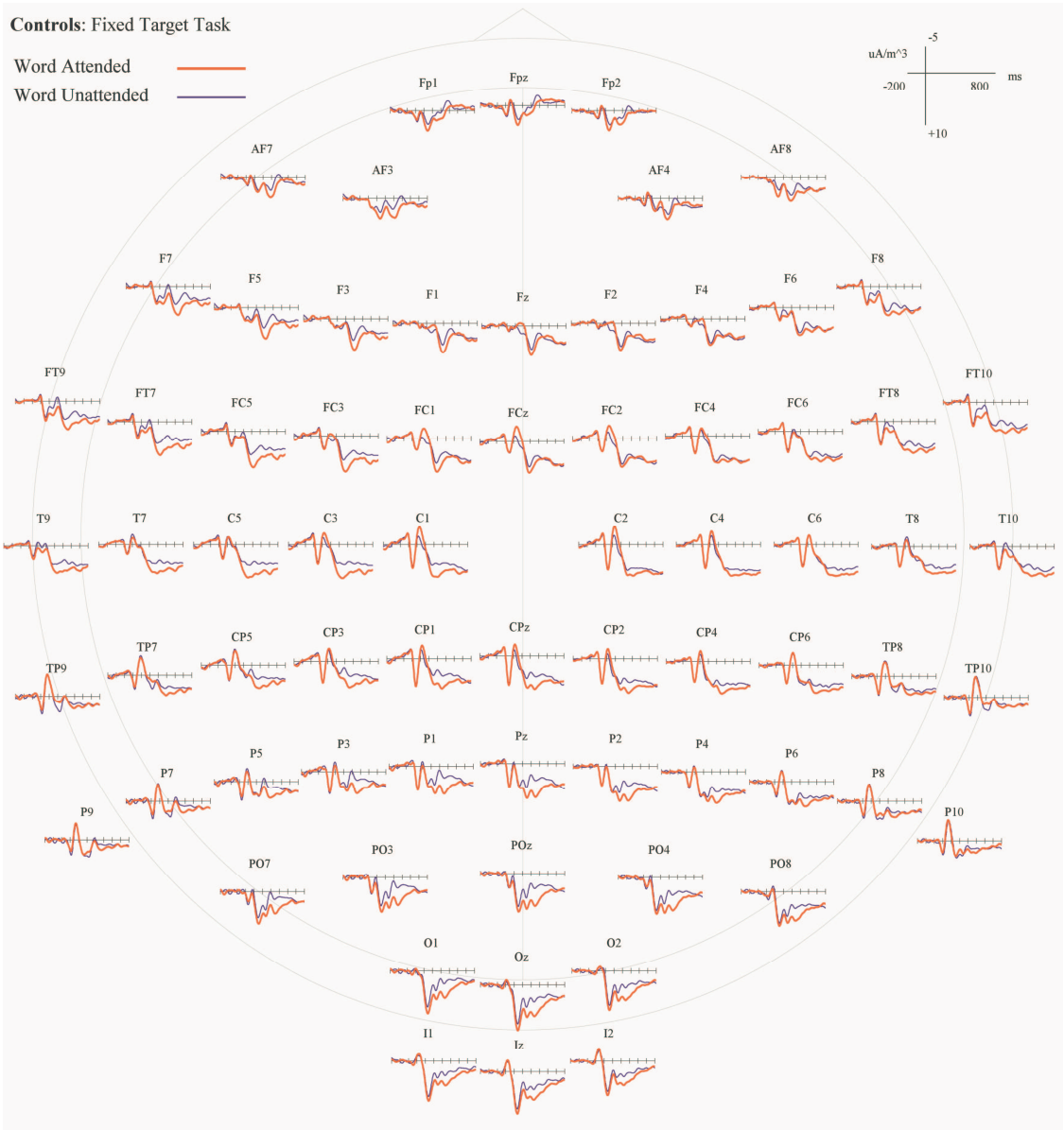

Figure 4-14. Event-related SCD in controls (n=10) at 70 scalp sites (-200 to 800 ms, 100 ms tick marks). Attended words clearly elicit larger positive SCD over occipito-parietal and left fronto-central regions at 300-600 ms.

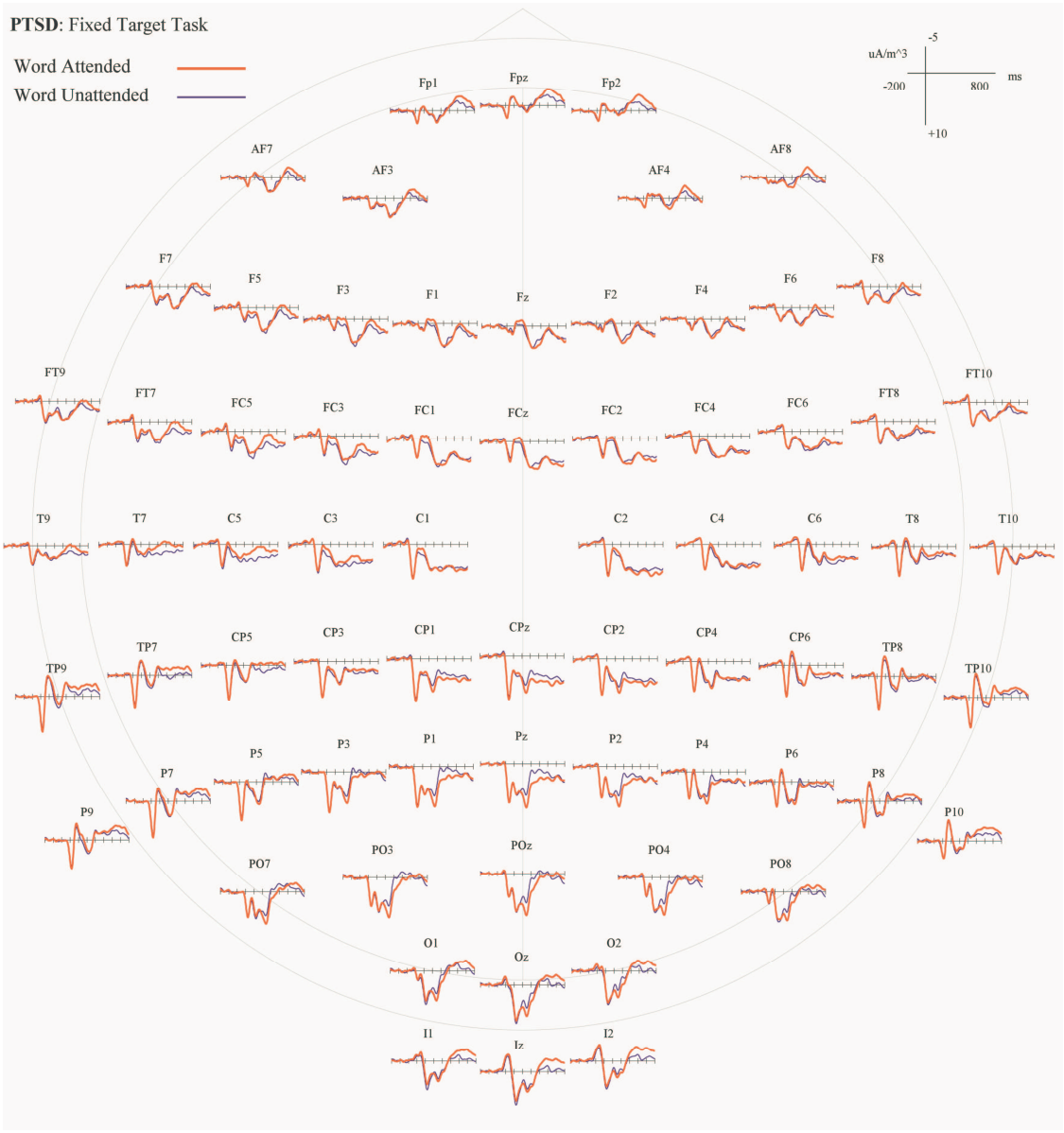

Figure 4-15. Event-related SCD in PTSD (n=10) at 70 scalp sites (-200 to 800 ms, 100 ms tick marks). Attended words elicit larger positive SCD over occipito-parietal regions at 300-600 ms. There are large event-related currents in response to visual word stimuli, but the attention differences are smaller in PTSD patients than controls.

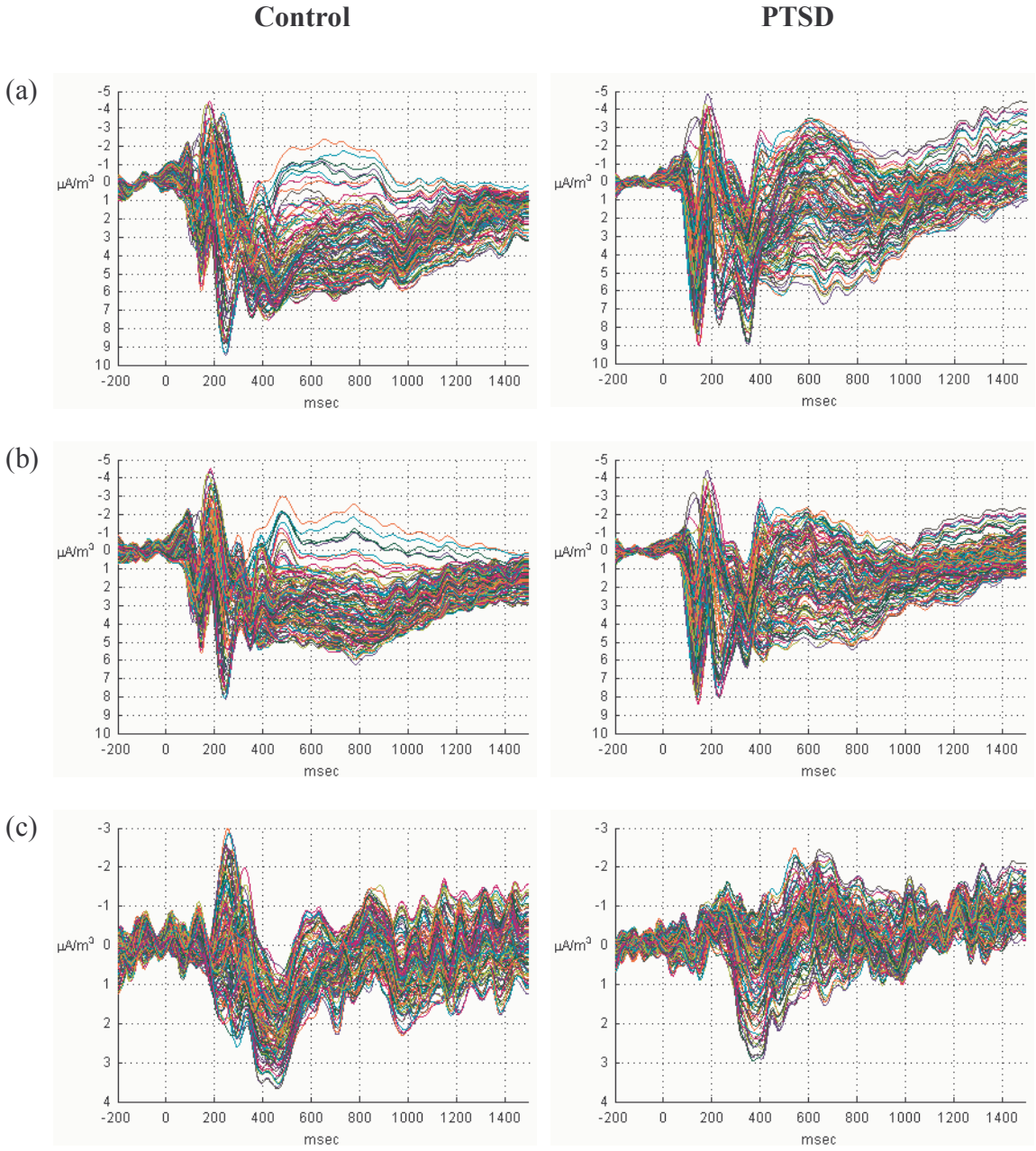

Figure 4-16. Event-related SCD waveforms at 124 scalp sites for controls (n=10) and PTSD patients (n=10): (a) attended common words, (b) unattended common words, (c) attended - unattended common words.

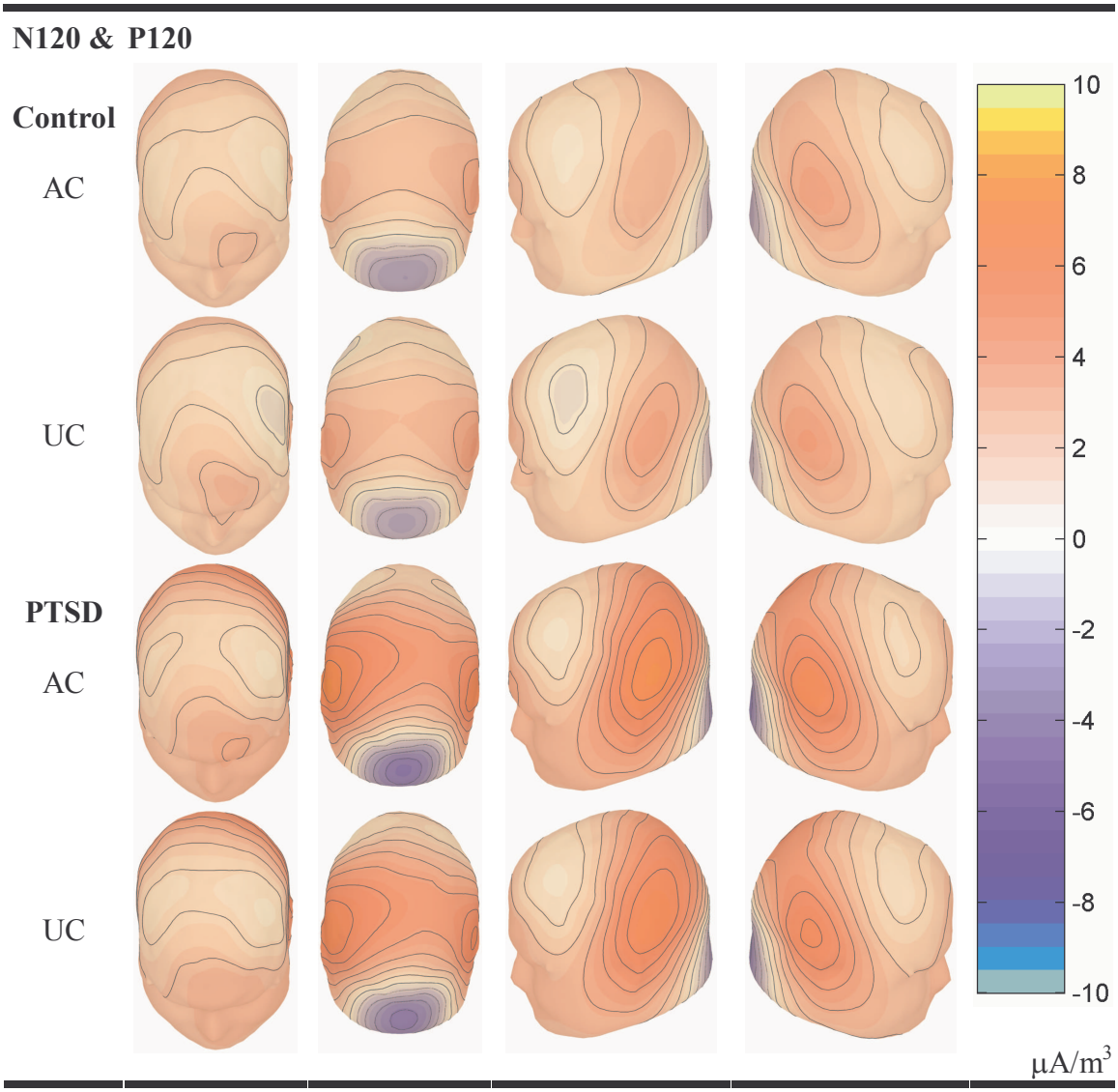

Figure 4-17. N120 & P120 SCD topography for controls (n = 10) and PTSD patients (n = 10) at 120 ms for both attended common (AC) and unattended common (UC) words (contours at 1 $\mu A/m^3$ intervals). See selected waveforms below.

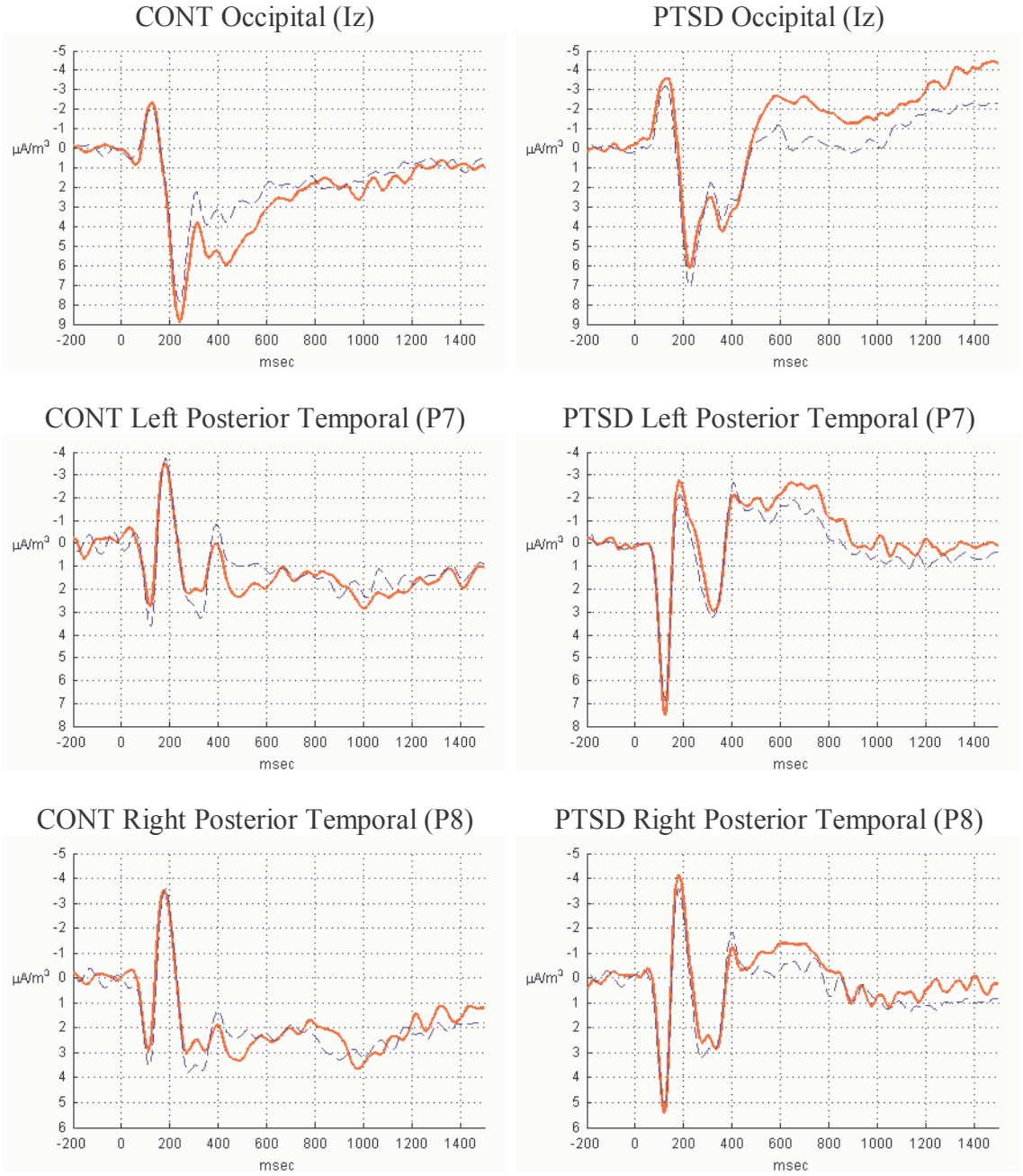

Figure 4-18. N120 & P120 SCD waveforms for controls (n = 10) and PTSD patients (n = 10) for both attended (red, solid) and unattended (blue, dash) common words. Note that the N120 at Iz is similar for both groups, while the P120 at P7/P8 is larger for patients. See the topography above.

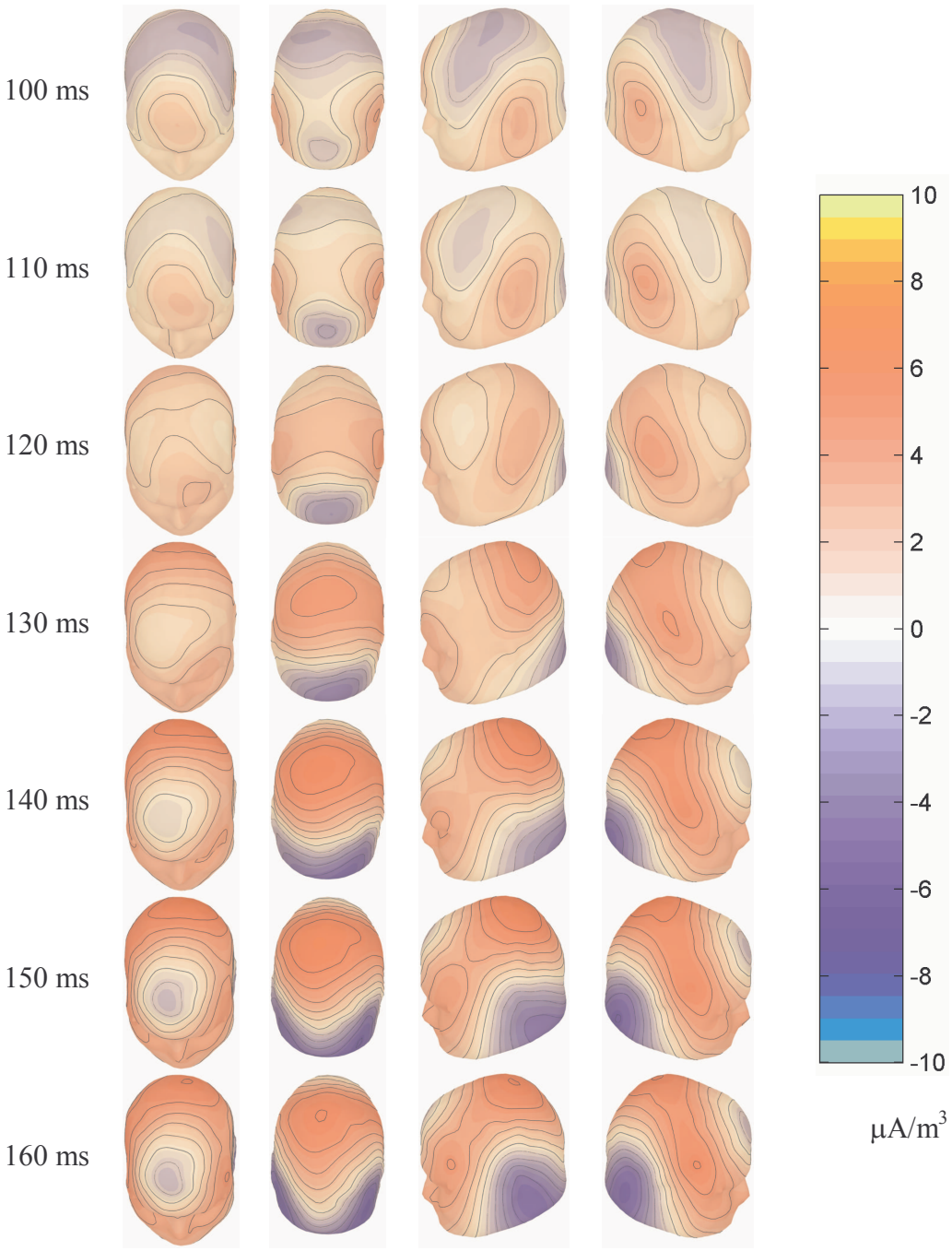

Figure 4-19. Dynamics of SCD topography for attended words from P120 to P150 components in controls (n=10; contours at 1 $\mu A/m^3$ intervals). The positive SCD over posterior temporal regions (P120) converged toward the medial parietal region (P150). Also, the negative SCD over the occipital region (N120) increased in amplitude and diverged into the posterior temporal regions (N180).

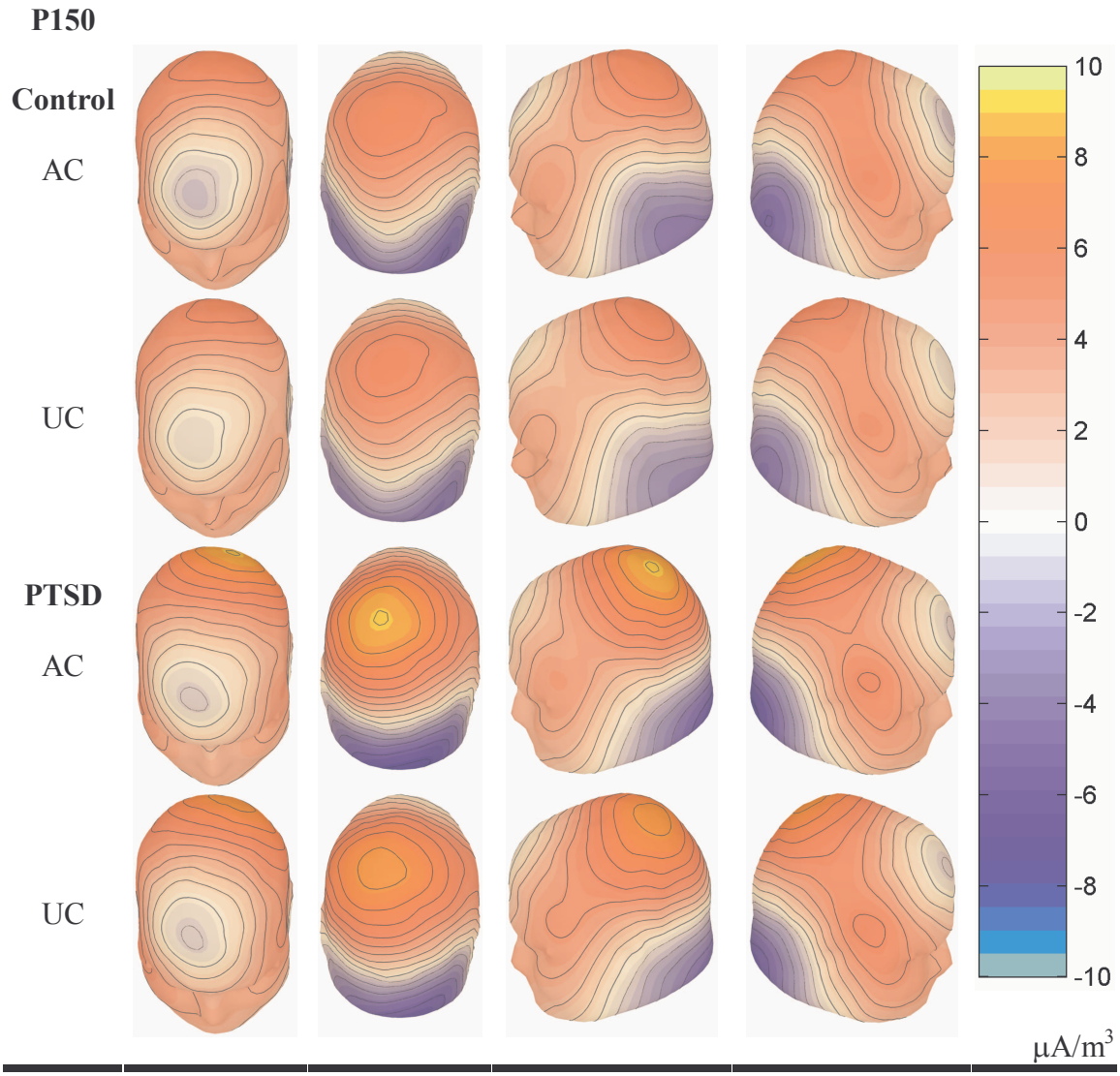

Figure 4-20. P150 SCD topography for controls (n = 10) and PTSD patients (n = 10) at 150 ms for both attended common (AC) and unattended common (UC) words (contours at 1 $\mu A/m^3$ intervals). See selected waveforms below.

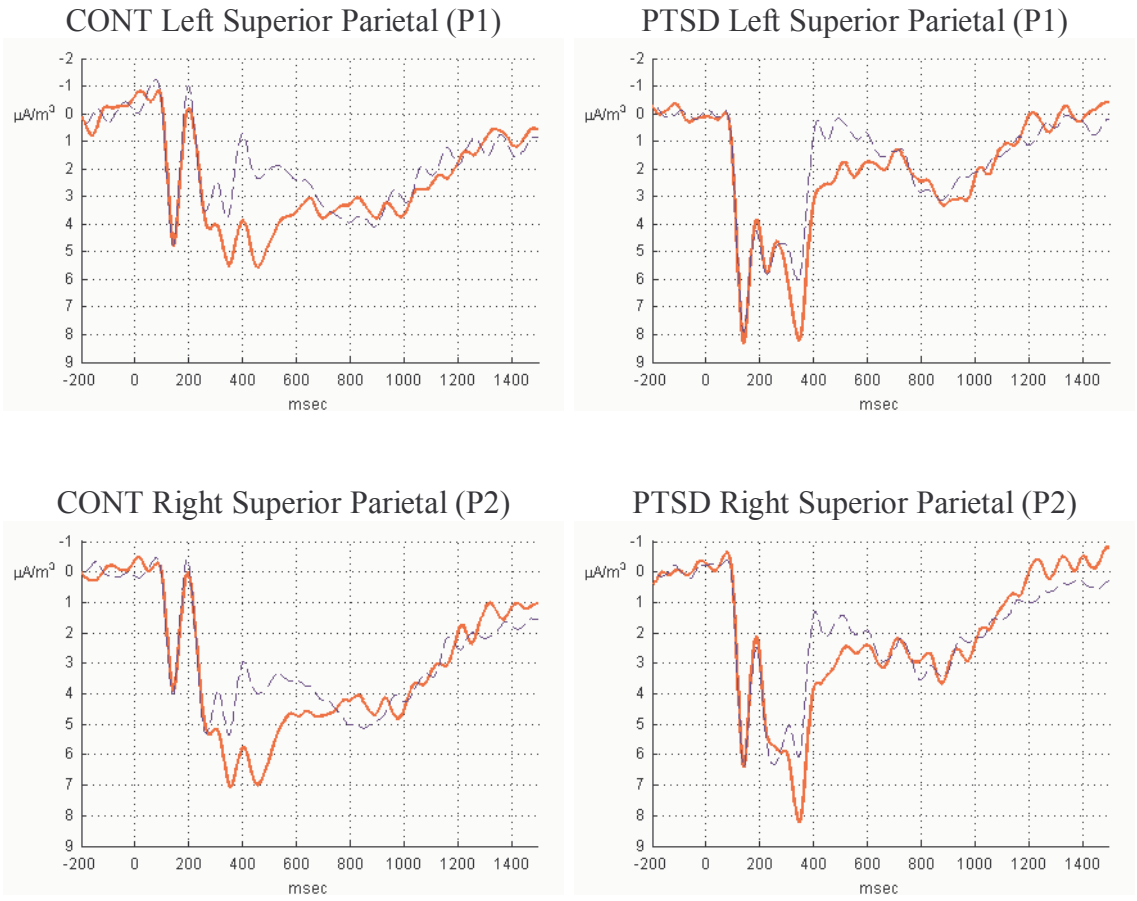

Figure 4-21. P150 SCD waveforms for controls (n = 10) and PTSD patients (n = 10) for both attended (red, solid) and unattended (blue, dash) common words (contours at 1 $\mu A/m^3$ intervals). There is similar amplitude for attended and unattended words, but note the larger amplitude for patients and the left hemisphere. See the topography above.

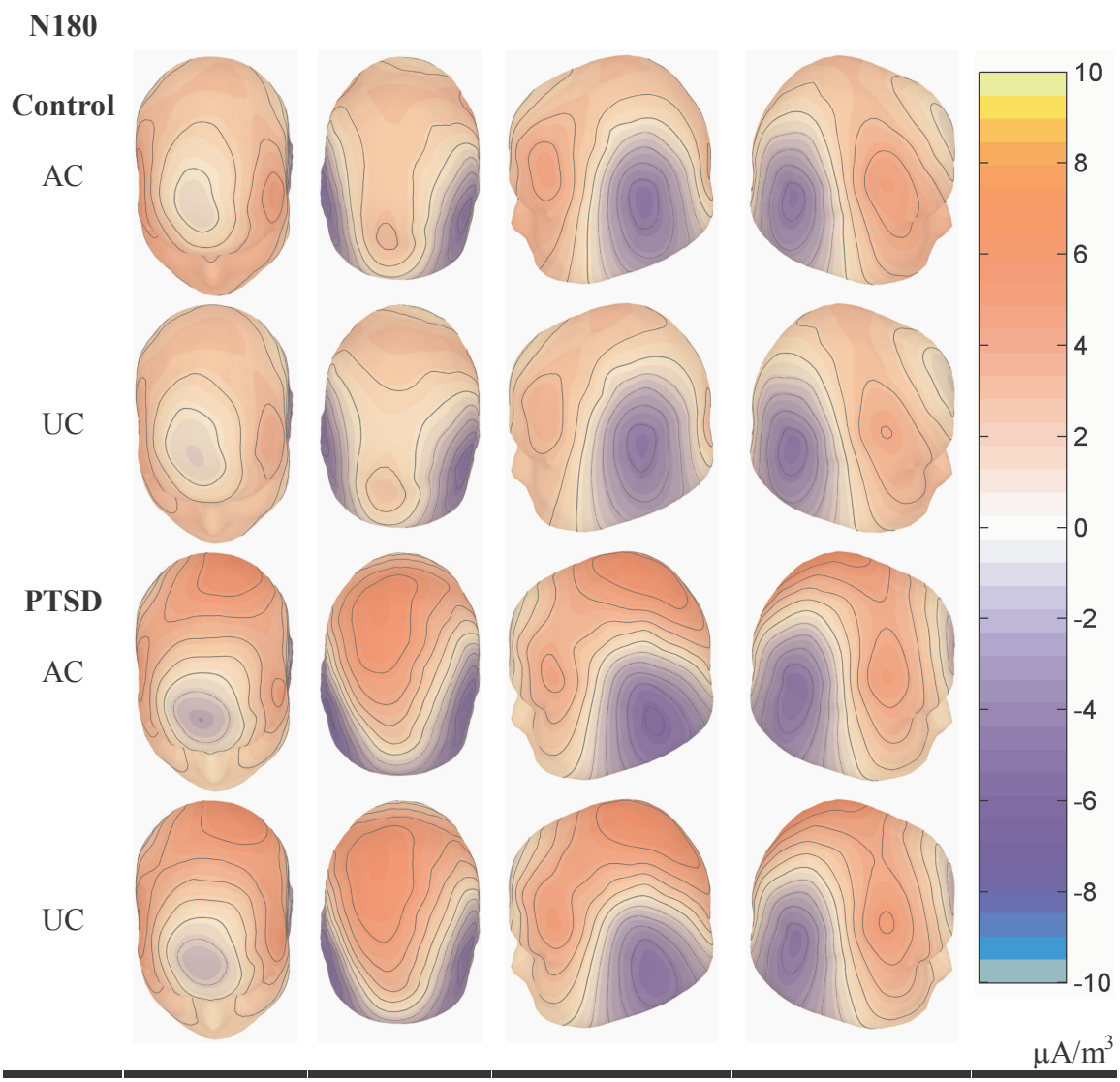

Figure 4-22. N180 SCD topography for controls (n = 10) and PTSD patients (n = 10) at 180 ms for both attended common (AC) and unattended common (UC) words (contours at 1 $\mu A/m^3$ intervals). See selected waveforms below.

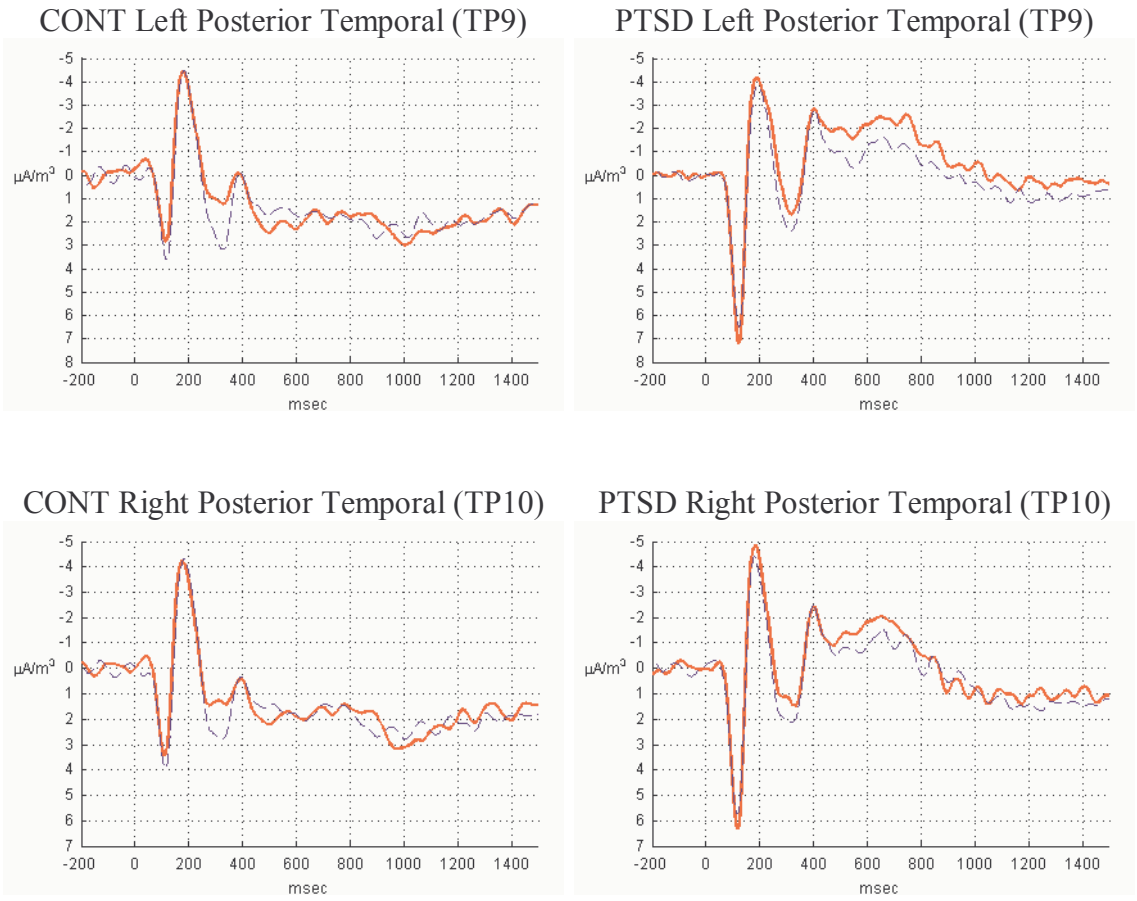

Figure 4-23. N180 SCD waveforms for controls (n = 10) and PTSD patients (n = 10) for both attended (red, solid) and unattended (blue, dash) common words. Note the similar amplitude for attended and unattended words and also for both groups. See the topography above.

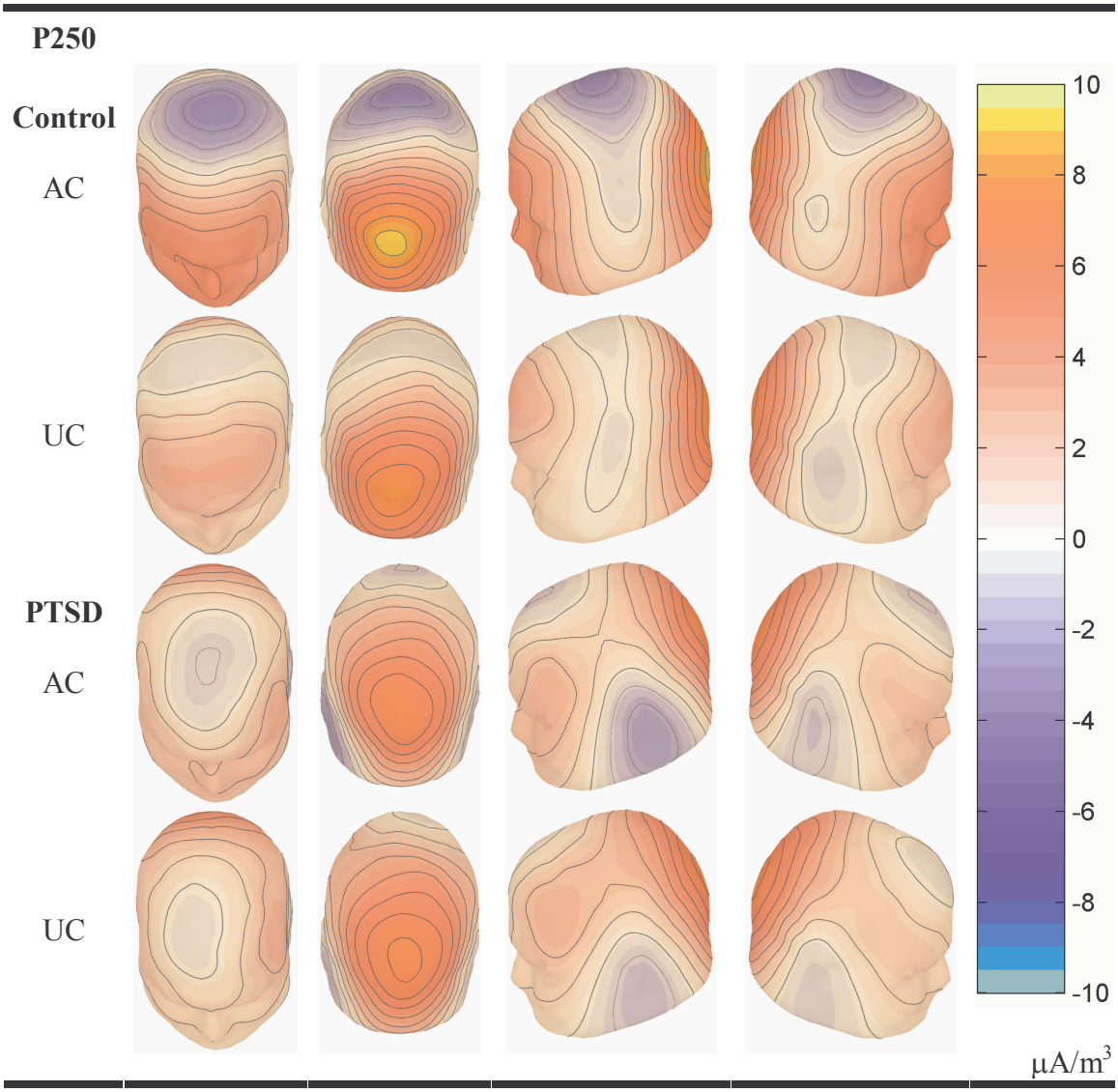

Figure 4-24. P250 SCD topography for controls (n = 10) and PTSD patients (n = 10) at 250 ms for both attended common (AC) and unattended common (UC) words (contours at 1 $\mu A/m^3$ intervals). See selected waveforms below.

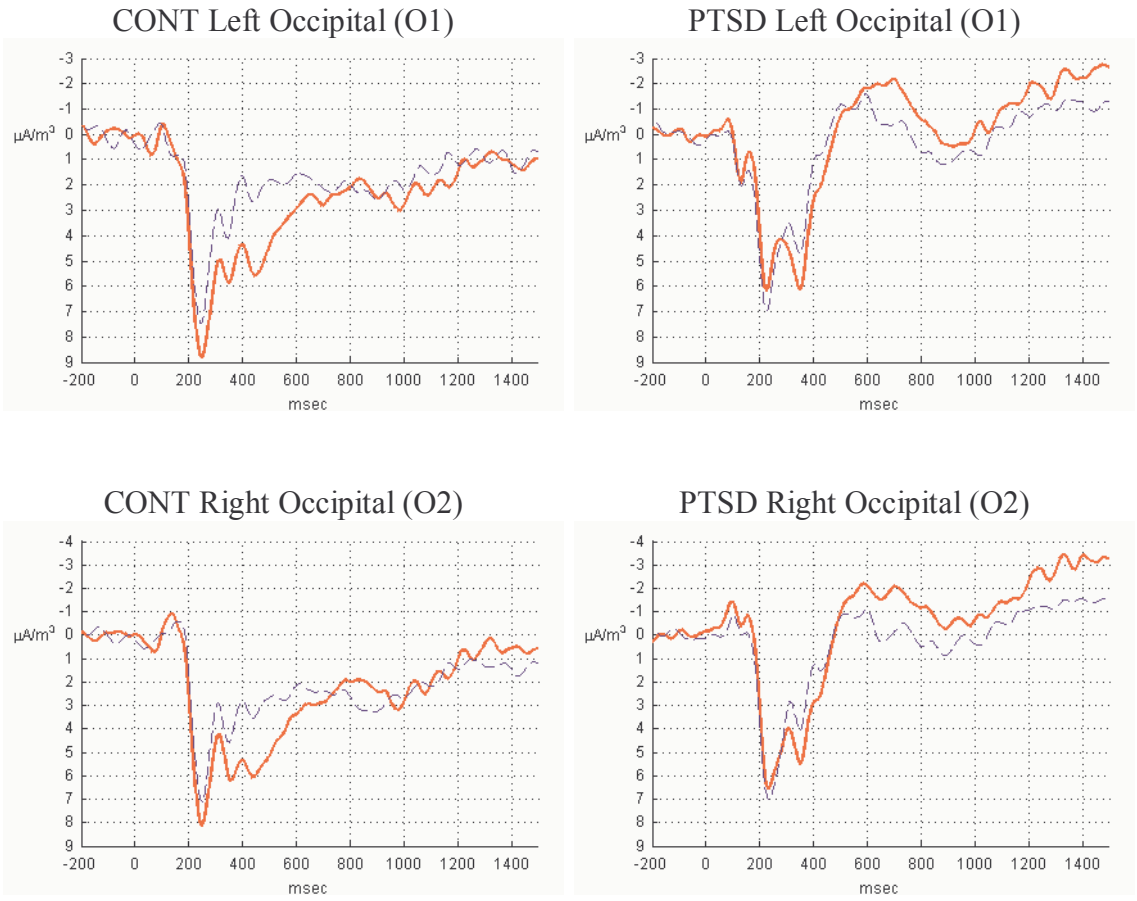

Figure 4-25. P250 SCD waveforms for controls (n = 10) and PTSD patients (n = 10) for both attended (red, solid) and unattended (blue, dash) common words. Note a possible interaction of group by attention, with amplitude greater for attended and unattended words in controls and *vice versa* for patients. See the topography above.

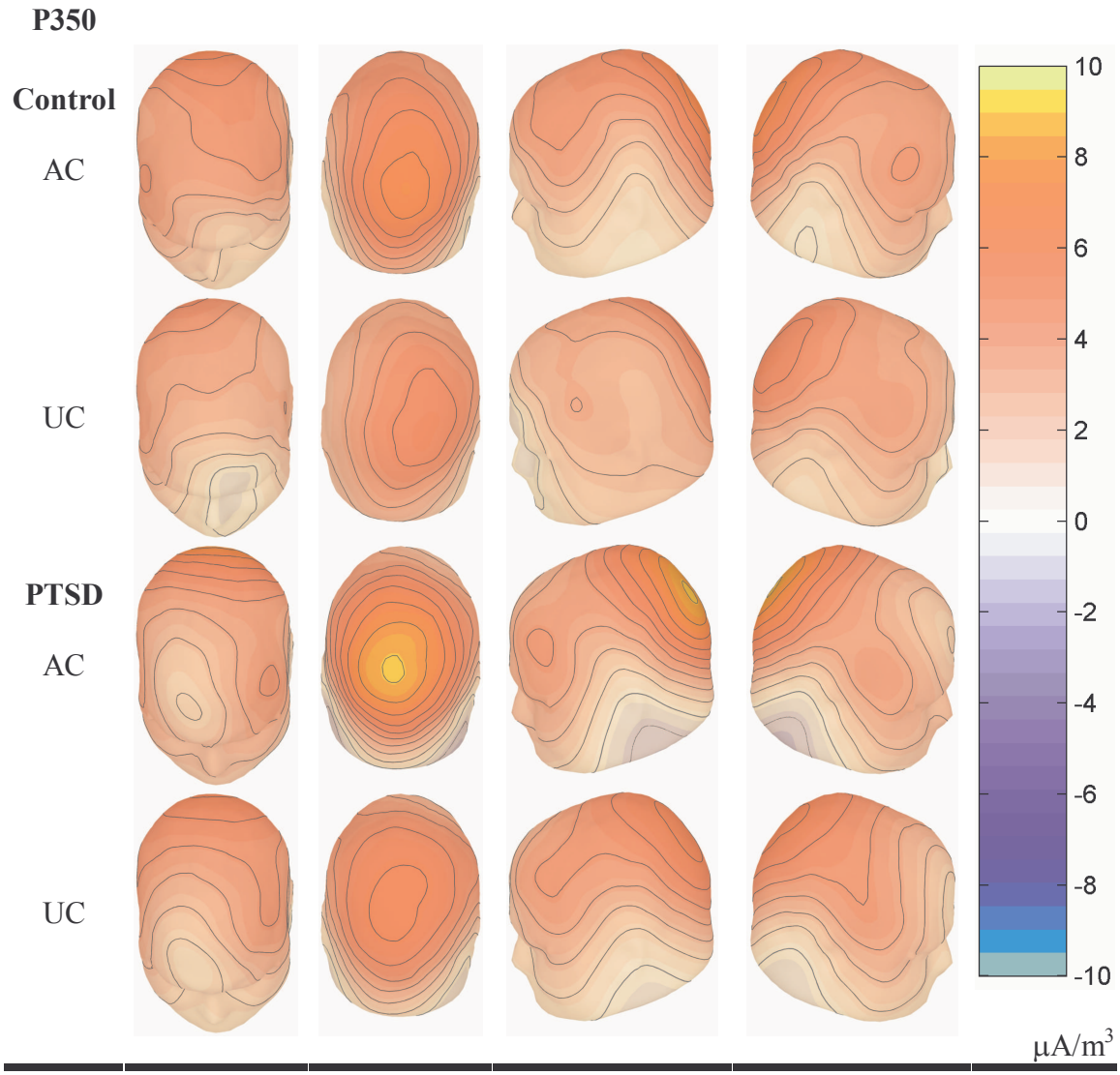

Figure 4-26. P350 SCD topography for controls (n = 10) and PTSD patients (n = 10) at 350 ms for both attended common (AC) and unattended common (UC) words (contours at 1 $\mu A/m^3$ intervals). See selected waveforms below.

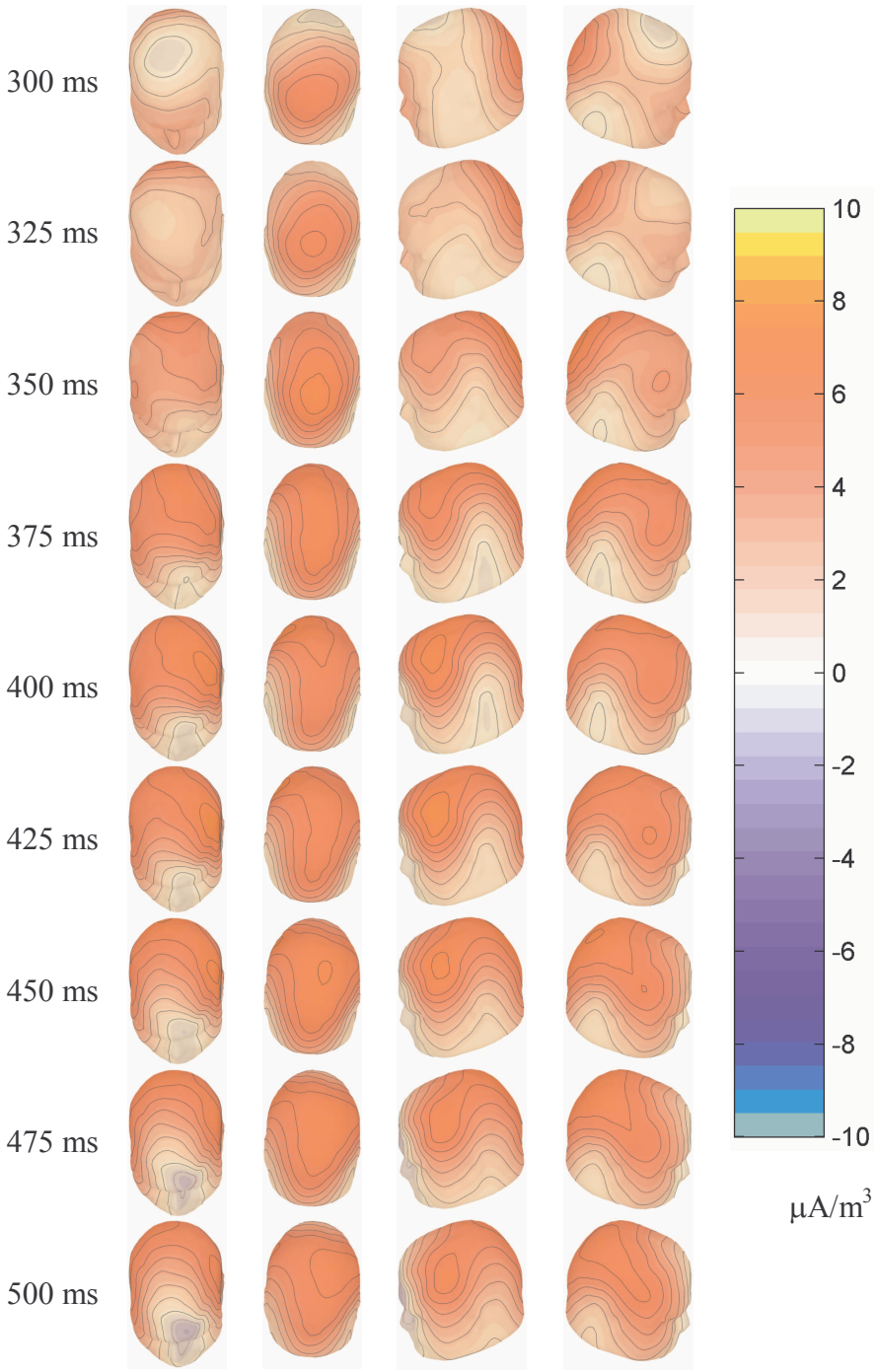

Figure 4-27. Dynamics of SCD topography for attended words from 300 to 500 ms in controls (n=10; contours at 1 μA/m^3 intervals). The topographic dynamics indicated that the P350 at parietal regions was later coupled with activity at lateral frontal regions.

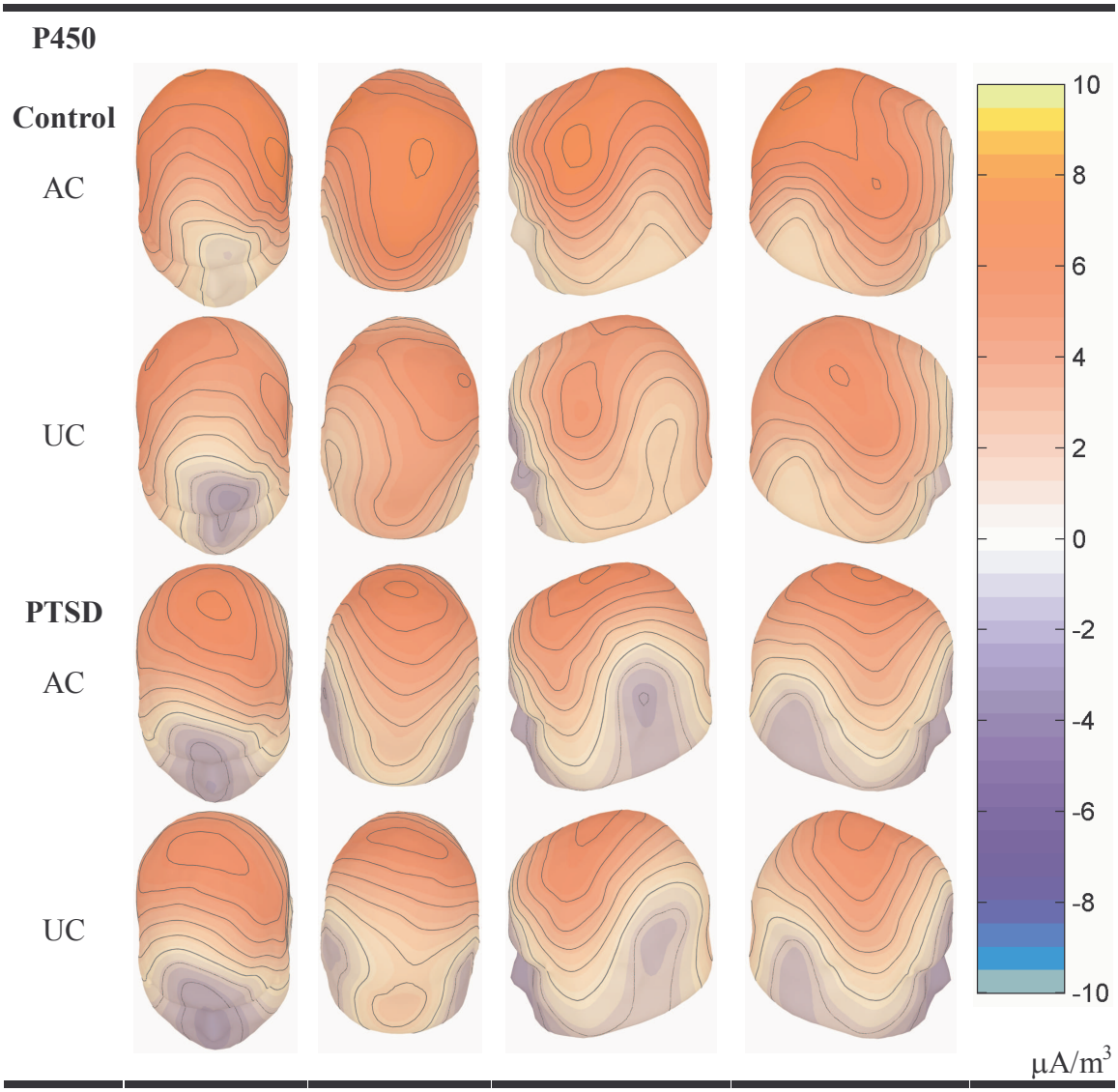

Figure 4-28. P450 SCD topography for controls (n = 10) and PTSD patients (n = 10) at 450 ms for both attended common (AC) and unattended common (UC) words (contours at 1 $\mu A/m^3$ intervals). See selected waveforms below.

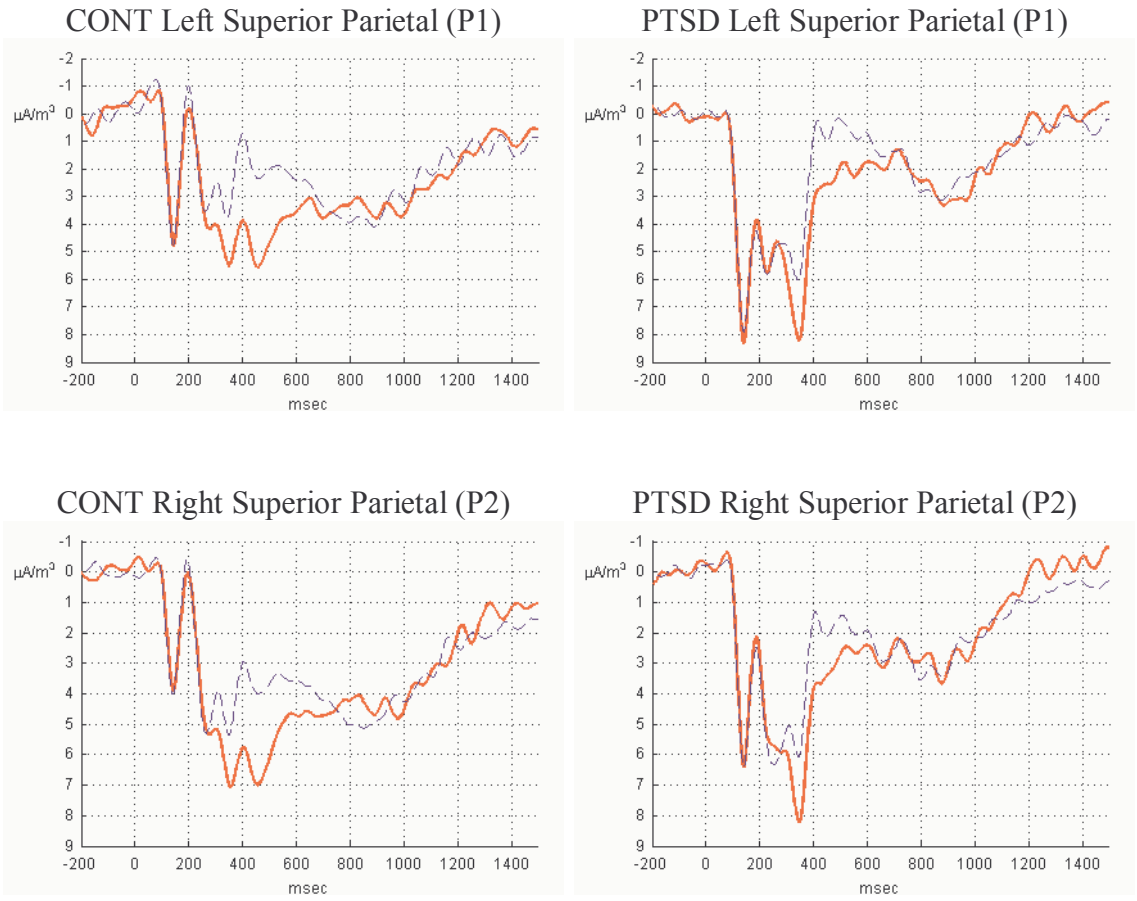

Figure 4-29. P350/P450 SCD waveforms at parietal sites for controls (n = 10) and PTSD patients (n = 10) for both attended (red, solid) and unattended (blue, dash) common words. A few features to note: (a) larger amplitude for attended than unattended words in controls and patients for the P350 (with larger amplitude, but similar condition differences in patients), (b) the P350 attention differences are further enhanced in the P450 for controls, but they are quickly resolved in patients, leaving no clear P450, and (c) although there is still an attention difference apparent at the latency of the P450 in patients, it is not associated with a P450 peak (only an N400, perhaps). See the topography above and frontal sites below.

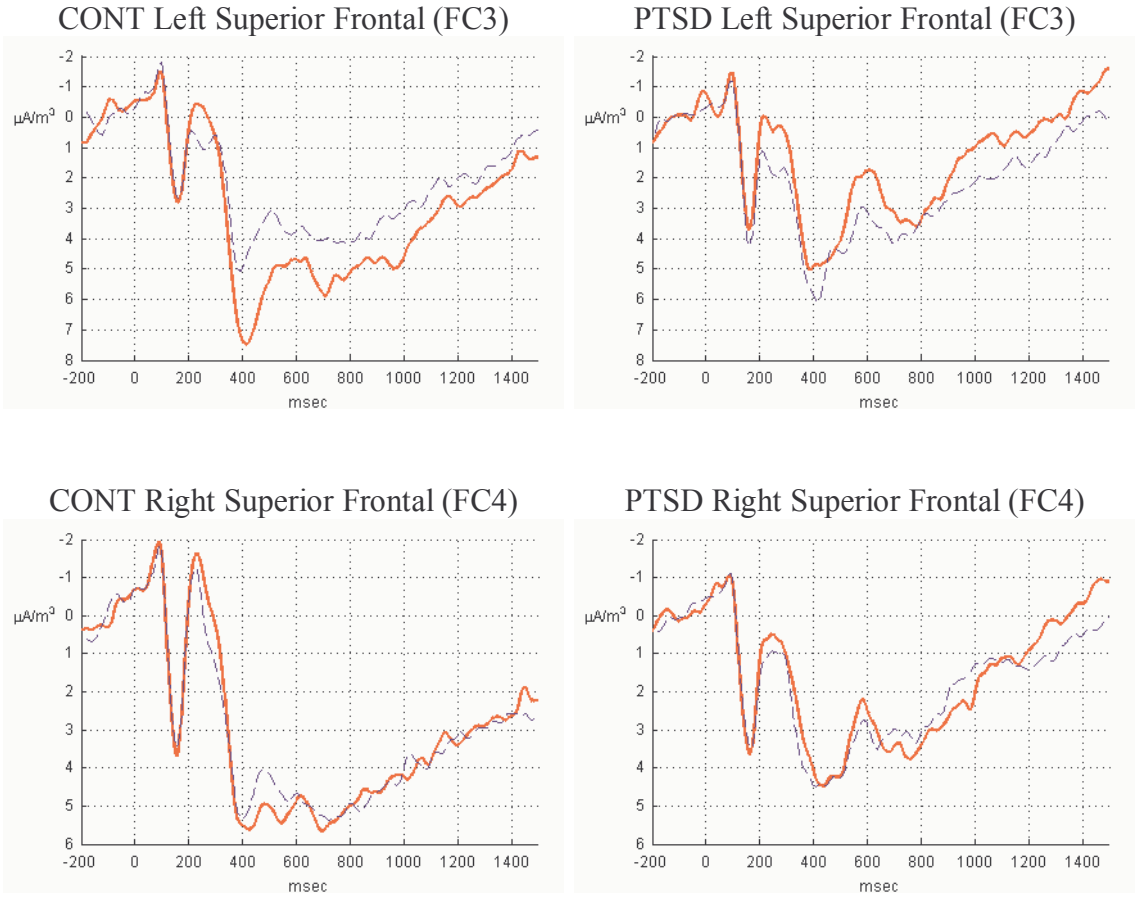

Figure 4-30. P450 SCD waveforms at frontal sites for controls (n = 10) and PTSD patients (n = 10) for both attended (red, solid) and unattended (blue, dash) common words. Note: the larger amplitude for attended than unattended words in controls over the left frontal region and the lack of similar differences in patients. Also note the smaller amplitude in patients than controls. See the topography and parietal sites above.

Table 4-6. SCD Summary Statistics for Attended and Unattended Common Words [a] (continued overleaf).

			Amplitude ($\mu A/m^3$)		Latency (ms)	
			CONT	PTSD	CONT	PTSD
N120	Left	AC	-6.26 (4.49)	-6.01 (10.96)	120.50 (36.13)	128.00 (25.49)
OC		UC	-5.84 (5.10)	-5.08 (10.18)	120.50 (35.88)	125.75 (25.22)
	Right	AC	-6.16 (4.01)	-7.32 (8.95)	128.25 (33.36)	140.00 (21.11)
		UC	-5.39 (4.63)	-6.67 (8.41)	121.75 (32.10)	137.50 (22.05)
P120	Left	AC	6.88 (6.07)	10.78 (9.30)	127.25 (22.00)	126.25 (16.30)
PT		UC	6.92 (5.94)	10.41 (8.50)	126.00 (20.55)	125.50 (16.74)
	Right	AC	5.85 (4.37)	8.83 (8.89)	121.75 (30.09)	120.25 (23.29)
		UC	5.83 (3.98)	8.27 (7.04)	118.75 (23.67)	118.75 (23.37)
P150	Left	AC	8.36 (6.48)	13.10 (9.42)	142.50 (20.51)	141.25 (21.99)
SP		UC	8.22 (6.70)	12.79 (9.05)	141.75 (19.08)	141.50 (24.81)
	Right	AC	7.03 (5.79)	11.79 (9.30)	140.75 (15.86)	139.25 (25.03)
		UC	7.29 (5.63)	11.57 (8.68)	146.00 (8.18)	137.25 (23.02)
N180	Left	AC	-8.22 (4.08)	-8.40 (4.76)	182.50 (28.28)	179.00 (24.95)
PT		UC	-8.40 (3.79)	-8.12 (4.41)	186.75 (30.30)	179.25 (23.48)
	Right	AC	-7.83 (3.78)	-8.04 (4.66)	179.25 (27.72)	173.00 (22.29)
		UC	-7.85 (3.57)	-7.81 (4.60)	187.75 (29.92)	174.00 (26.72)

[a] Values are mean (SD); AC = Attended Commons, UC = Unattended Commons; OC = occipital, PT = posterior temporal, SP = superior parietal; CONT, n = 10; PTSD, n = 10.

Table 4-6 (continued). SCD Summary Statistics for Attended and Unattended Common Words [a]

			Amplitude (μA/m^3)		Latency (ms)	
			CONT	PTSD	CONT	PTSD
P250	Left	AC	12.10 (6.54)	12.91 (5.99)	268.75 (56.07)	271.50 (51.36)
OC		UC	9.83 (5.11)	11.45 (7.09)	273.75 (53.27)	257.25 (45.33)
	Right	AC	10.84 (3.76)	11.89 (8.34)	253.25 (40.04)	260.00 (50.33)
		UC	10.12 (4.27)	11.82 (7.60)	259.25 (50.10)	249.25 (43.51)
P350	Left	AC	9.32 (5.54)	10.64 (7.38)	346.00 (20.89)	344.75 (20.39)
SP		UC	7.21 (4.16)	8.39 (7.99)	341.00 (14.92)	351.25 (17.17)
	Right	AC	10.10 (5.60)	10.89 (7.70)	350.25 (18.31)	348.00 (17.19)
		UC	7.88 (4.62)	8.54 (7.99)	343.75 (16.51)	352.00 (12.29)
P450	Left	AC	10.98 (4.37)	8.80 (4.26)	413.75 (40.52)	439.25 (53.03)
SF		UC	7.43 (3.24)	8.24 (4.64)	403.75 (32.04)	422.00 (54.59)
	Right	AC	9.36 (3.19)	8.29 (4.30)	426.75 (59.18)	453.50 (45.33)
		UC	7.54 (3.82)	7.48 (4.36)	408.75 (37.03)	414.50 (60.02)
P450	Left	AC	9.89 (4.36)	5.77 (5.88)	458.00 (34.05)	445.00 (42.57)
SP		UC	6.18 (3.40)	5.04 (5.87)	464.00 (30.37)	440.75 (42.07)
	Right	AC	10.07 (4.53)	6.94 (5.86)	448.75 (46.36)	449.50 (34.21)
		UC	6.55 (2.80)	6.08 (5.88)	467.50 (40.45)	454.25 (37.82)

[a] Values are mean (SD); AC = attended commons; UC = unattended commons; OC = occipital, SP = superior parietal, SF = superior frontal; CONT, n = 10; PTSD, n = 10.

Table 4-7. Inferential Statistics for Selective Attention SCD Components [a]

SCD		GP	SA	GPxSA	HS	GPxHS	SAxHS	GPxSAxHS
N120	Amp	0.01	4.57*	0.09	1.40	3.07	0.03	2.32
OC	Lat	0.75	1.72	0.04	2.23	0.45	0.58	0.50
P120	Amp	1.11	0.75	0.81	4.84*	0.49	0.13	0.04
PT	Lat	0.01	1.52	0.14	1.51	0.00	0.23	0.04
P150	Amp	1.77	0.23	0.57	9.73**	0.03	1.37	0.56
SP	Lat	0.12	0.26	1.37	0.09	0.47	0.45	2.19
N180	Amp	0.00	0.11	0.60	0.23	0.01	0.01	0.07
PT	Lat	0.52	1.73	1.16	0.55	0.24	2.00	0.98
P250	Amp	0.24	7.29*	0.76	0.40	0.01	2.12	0.01
OC	Lat	0.05	0.27	1.79	3.98	0.18	0.04	0.01
P350	Amp	0.12	13.91**	0.01	1.48	0.47	0.21	0.00
SP	Lat	0.29	0.01	3.49	4.47*	0.33	0.76	0.05
P450	Amp	0.13	26.21***	9.30**	4.12	0.03	1.49	2.64
SF	Lat	1.17	3.98	0.45	1.62	0.33	1.95	0.42
P450	Amp	1.21	8.61**	3.52 †	2.52	0.94	0.00	0.06
SP	Lat	0.84	0.87	0.81	0.17	0.62	1.36	0.04

[a] Values are $F[1,18]$, GP = group, SA = selective attention, HS = hemisphere.

* $p<.05$, ** $p<.01$, *** $p<.001$, *2-tailed*; † $p<.05$, †† $p<.01$, ††† $p<.001$, *1-tailed*.

4.5.5.1 N120 SCD

The N120 component was an occipital peak (see Figure 4-17 & Figure 4-18). N120 peak amplitude was largest over the occipital region between 80-180 ms (see Table 4-6). ANOVA indicated a significant attention effect on N120 amplitude (see Table 4-7). The mean N120 peak was larger (more negative) for attended than unattended words (M = -0.69 μA/m^3, SE = 0.32 μA/m^3, $p<.05$).

4.5.5.2 P120 SCD

The P120 component comprised large positive peaks over bilateral posterior temporal regions (see Figure 4-17 & Figure 4-18). P120 peak amplitude was largest at bilateral posterior temporal regions between 80-180 ms (see Table 4-6). ANOVA

indicated a significant hemisphere difference in P120 amplitude (see Table 4-7). The mean P120 peak amplitude was larger over the left than the right posterior temporal region (M = 1.55 μA/m^3, SE = 0.71 μA/m^3, p<.05).

4.5.5.3 P150 SCD

The P150 was a positive peak over the parietal region at 120-180 ms (see Figure 4-20), with larger amplitude for patients than controls (see Figure 4-21). The P150 peak amplitude was largest at the superior parietal region between 80-180 ms (see Table 4-6, note large variability in peak amplitude). ANOVA indicated a significant hemisphere difference in P150 amplitude (see Table 4-7). The mean P150 peak amplitude was greater over the left than the right superior parietal region (M = 1.20 μA/m^3, SE = 0.38 μA/m^3, p<.01).

4.5.5.4 N180 SCD

The N180 was a negative peak at 170-180 ms over bilateral posterior temporal regions (see Figure 4-22 & Figure 4-23). The N180 peak was largest at bilateral posterior temporal regions between 120-240 ms (see Table 4-6). ANOVA indicated no significant differences in N180 amplitude and latency (see Table 4-7).

4.5.5.5 P250 SCD

The P250 arose over occipito-parietal regions at 200-250 ms (see Figure 4-24 & Figure 4-25). The grand mean waveforms and topography indicate that P250 amplitude is larger for attended than unattended words, especially for controls. P250 peak amplitude was largest at the occipital region between 180-350 ms (see Table 4-6). ANOVA indicated a significant effect of attention on P250 amplitude (see Table 4-7). The mean P250 peak amplitude was greater for attended than unattended words (M = 1.13 μA/m^3, SE = 0.42 μA/m^3, p<.05).

4.5.5.6 P350 SCD

The P350 was a positive peak over the parietal region (see Figure 4-26). P350 peak amplitude was largest at the superior parietal region between 300-380 ms (this time window was designed to exclude the latter P450). The sample means indicated that P350 amplitude was greater for attended than unattended words and also larger in patients than controls (see Figure 4-26, Figure 4-29 & Table 4-6). ANOVA indicated a significant effect of attention on P350 amplitude and a significant difference between hemispheres in P350 latency (see Table 4-7). The mean P350 peak amplitude was larger for attended than unattended words (M = 2.23 μA/m^3, SE = 0.60 μA/m^3, p<.01). The mean P350 peak latency arose earlier over the left than the right superior parietal region (M = -2.75 ms, SE = 1.30 ms, p<.05).

4.5.5.7 P450 SCD

The P450 was a large positive peak over parietal and frontal regions between 350-450 ms (see Figure 4-28, Figure 4-29 & Figure 4-30). P450 peak amplitude was largest at bilateral superior frontal and superior parietal regions between 300-525 ms, with greater amplitude for attended than unattended words, especially for controls (see Table 4-6).

Superior frontal: ANOVA indicated a significant interaction of group and attention on P450 amplitude (see Table 4-7). The mean P450 peak amplitude was larger for attended than unattended words over bilateral superior frontal regions for controls (M = 2.67 μA/m^3, SE = 0.47 μA/m^3, p<.001), but not for patients (M = 0.68 μA/m^3, SE = 0.47 μA/m^3, *ns*).

Superior parietal: The sample means indicated greater P450 for attended than unattended stimuli, especially for controls (see Table 4-6). A three-way ANOVA indicated a significant interaction of group and attention on P450 amplitude (see Table

4-7). The mean P450 peak amplitude was larger for attended than unattended words over the superior parietal region for controls (M = 3.61 μA/m^3, SE = 1.06 μA/m^3, p<.01), but not for patients (M = 0.79 μA/m^3, SE = 1.06 μA/m^3, *ns*).

4.5.5.8 Summary of SCD Findings

There were significant attention differences in the following SCD components:

- occipital N120 was larger for attended words at 120-140 ms,
- occipital P250 was larger for attended words at 250-275 ms,
- superior parietal P350 was larger for attended words at 340-355 ms, and
- superior parietal and superior frontal P450 was larger for attended words at 410-470 ms in controls, but not patients.

4.5.6 SCD Difference Wave Components

The attention difference waves demonstrate two clear components: (a) a negative peak at 250 ms (ND250) and (b) a positive peak at 400 ms (PD400; see Figure 4-16). Both groups demonstrated a negative difference peak over the central regions at 200-350 ms (ND250 SCD) and a positive difference peak over the parietal and left frontal regions at 300-500 ms (PD400 SCD; see Figure 4-31, Figure 4-32 & Figure 4-33). The grand mean waveforms indicate that these component peaks were larger for controls than patients. The summary statistics for these components are given in Table 4-8 and the inferential statistics are described below (see Table 4-9).

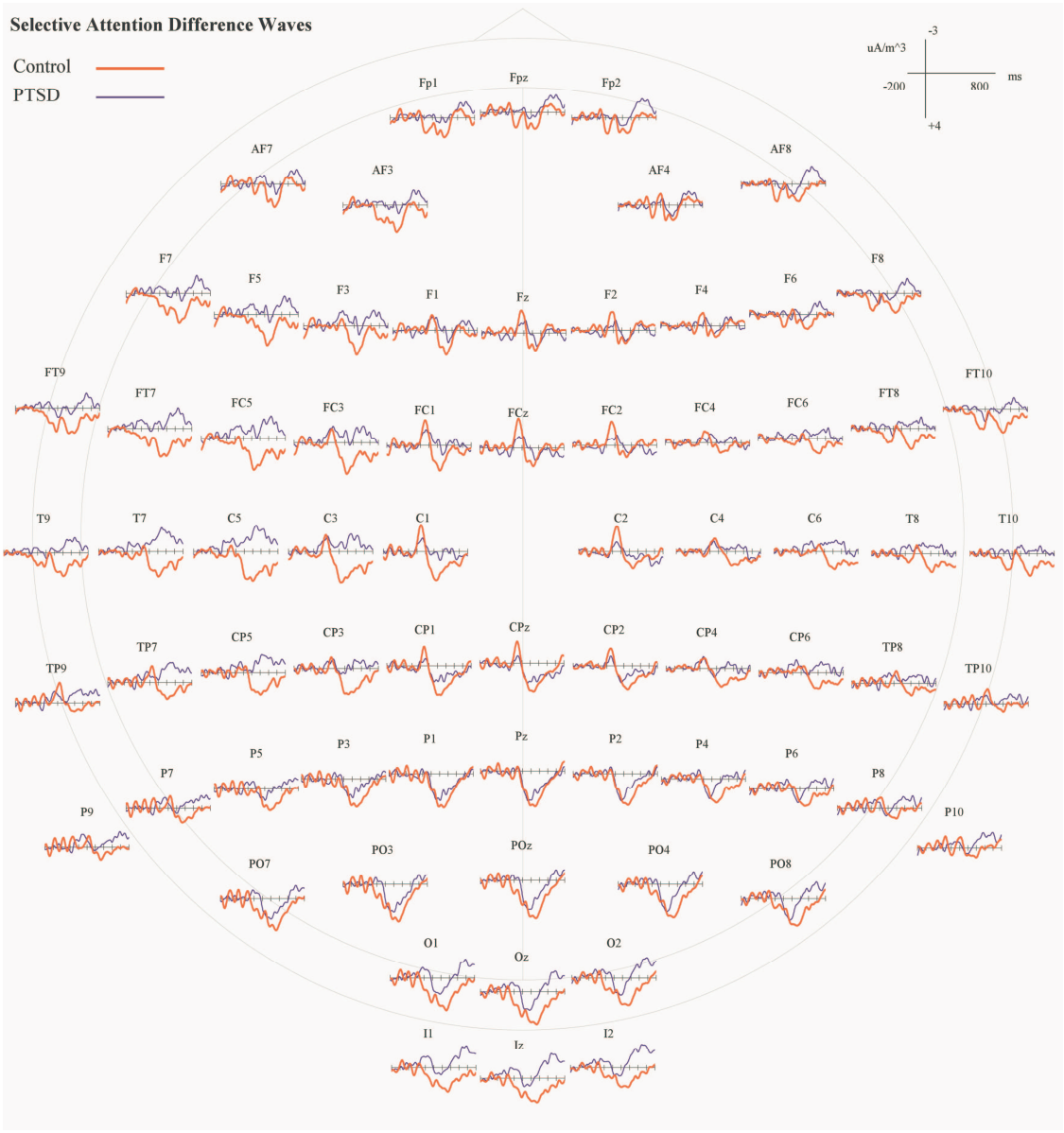

Figure 4-31. SCD waveforms at 70 scalp sites for the attention difference condition in controls (n = 10) and PTSD patients (n = 10; -200 to 800 ms, 100 ms tick marks).

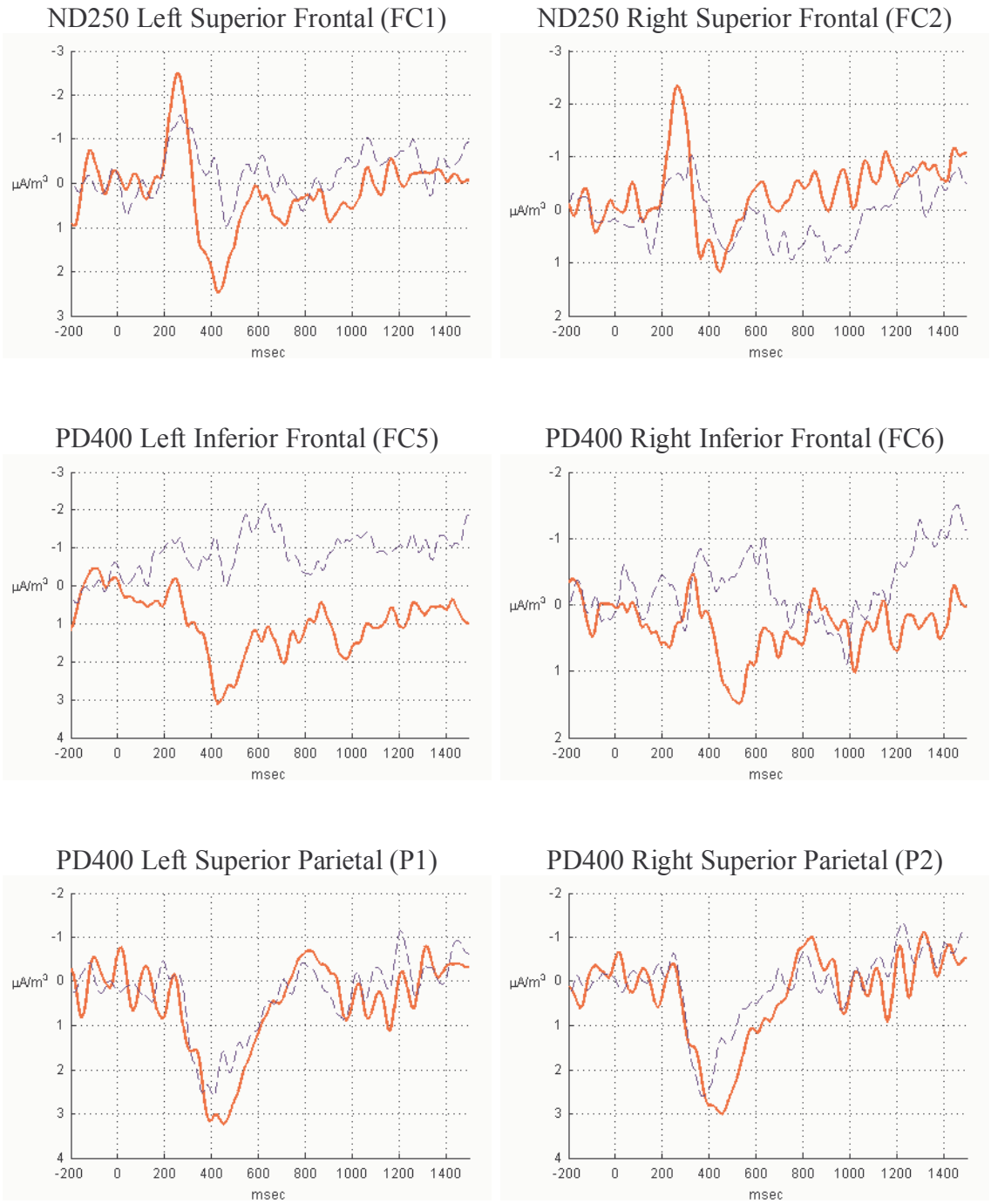

Figure 4-32. SCD attention difference waveforms for controls (n = 10; red, solid) and PTSD patients (n = 10; blue, dash). Note the ND250 at frontal regions and the PD400 at frontal and parietal regions.

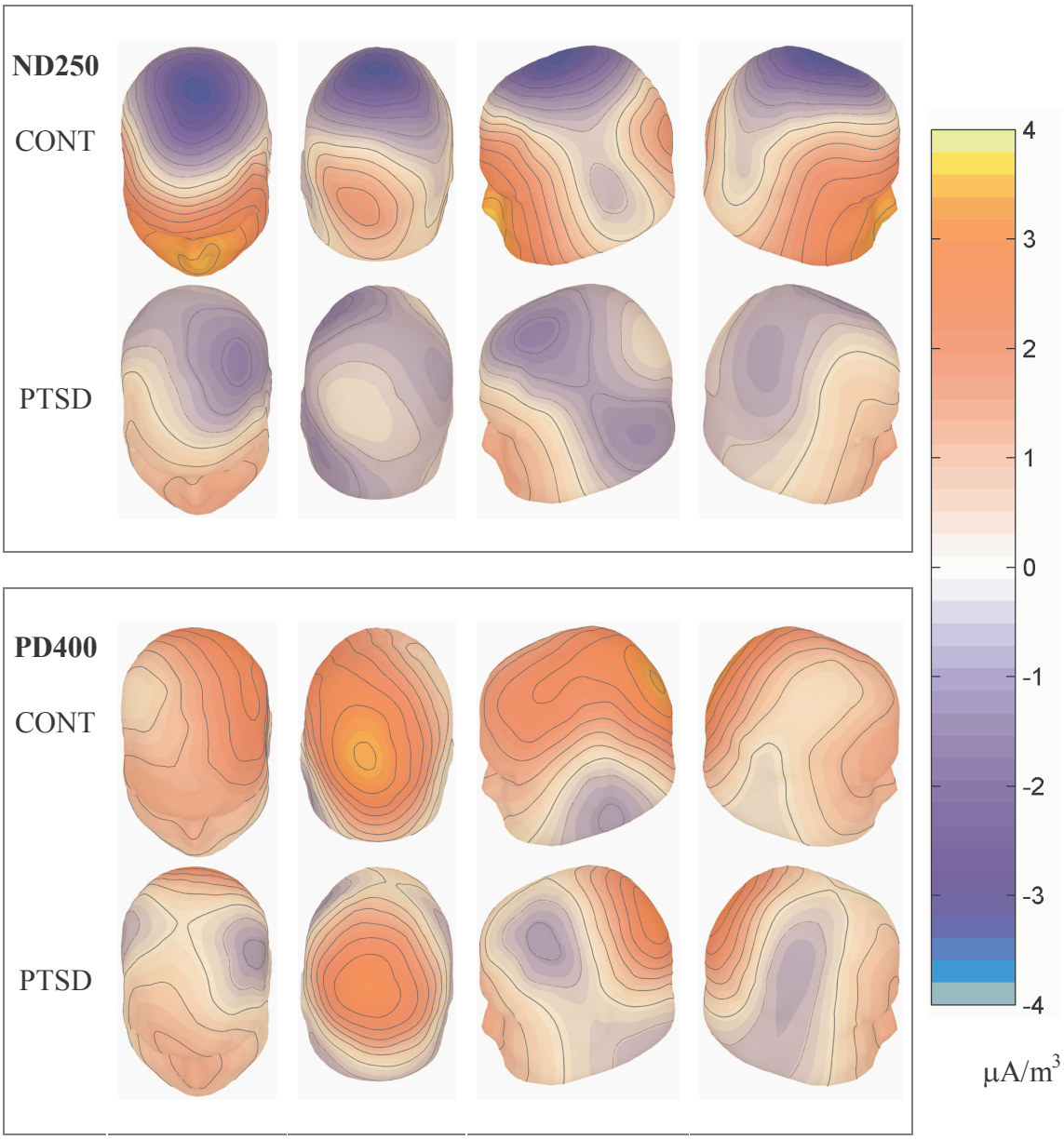

Figure 4-33. ND250 and PD400 SCD topography for controls (n = 10) and PTSD patients (n = 10; contours at 0.5 $\mu A/m^3$ intervals). The ND250 is shown at 260 ms and the PD400 at 400 ms. Note the similar topography for each group and that both components are larger in controls than patients. Note the lack of PD400 over left frontal regions in patients.

Table 4-8. SCD Summary Statistics for Attended - Unattended Common Words [a]

		Amplitude ($\mu A/m^3$)		Latency (ms)	
		CONT	PTSD	CONT	PTSD
ND250	Left	-3.72 (2.36)	-3.57 (1.83)	270.75 (26.98)	291.00 (42.89)
SF	Right	-4.31 (2.28)	-2.90 (1.68)	301.75 (48.22)	309.50 (53.12)
PD400	Left	5.00 (2.81)	2.48 (1.79)	443.50 (29.23)	451.00 (41.35)
SF	Right	3.59 (1.37)	2.77 (1.95)	442.50 (60.09)	475.75 (54.65)
PD400	Left	5.48 (2.44)	4.26 (2.91)	437.50 (46.84)	434.00 (73.01)
SP	Right	4.71 (2.88)	4.40 (2.82)	453.00 (52.23)	443.25 (67.36)

[a] Values are mean (SD); SP = superior parietal, SF = superior frontal; CONT, n = 10; PTSD, n = 10.

Table 4-9. Inferential Statistics for Selective Attention SCD Difference Components [a]

SCD		GP	HS	GPxHS
ND250	Amp	0.93	0.01	2.09
SF	Lat	0.73	5.27*	0.34
PD450	Amp	5.59*	0.92	2.14
SF	Lat	1.12	1.59	1.87
PD450	Amp	0.42	0.62	1.32
SP	Lat	0.07	1.69	0.11

[a] Values are $F[1,18]$, GP = group, HS = hemisphere.

* $p<.05$, ** $p<.01$, *** $p<.001$, *2-tailed*; † $p<.05$, †† $p<.01$, ††† $p<.001$, *1-tailed*.

4.5.6.1 ND250 SCD

A negative difference peak appeared at 200-300 ms, located over superior fronto-central regions. The ND250 peak was measured between 200-400 ms and found to be largest at superior frontal regions (see Table 4-8). ANOVA indicated a significant hemisphere difference in ND250 latency (see Table 4-9). ND250 arose earlier over the left than the right superior frontal region (M = -24.75 ms, SE = 10.78 ms, $p<.05$).

4.5.6.2 PD400 SCD

A large positive difference peak appeared at 350-550 ms over the parietal region. Specific research hypothesis also suggested analysis of the superior frontal region. PD400 peaks were measured between 350-550 ms over superior parietal and superior frontal regions (see Table 4-8).

Superior frontal: ANOVA indicated a significant group difference in PD400 amplitude (see Table 4-9). The mean PD400 peak amplitude was larger for controls than patients ($M = 1.67$, $SE = 0.71$, $p<.05$).

Superior parietal: ANOVA indicated no significant differences (see Table 4-9).

4.5.6.3 Summary of SCD difference waves

The PD400 was a large positive difference over parietal and frontal regions that peaked at 430-475 ms. The PD400 was larger for controls than patients over the superior frontal region.

4.6 DISCUSSION

4.6.1 Overview

There were clear early attention effects and also later differences in stimulus evaluation in the scalp electrical components in this study. The early effects were found between 80-200 ms over the occipital and frontal regions. These findings include enhanced amplitude for attended words in an occipital N120 SCD and N150 ERP and a superior frontal P150 ERP. These early attention effects represent modulations of brain activity engaged in stimulus detection and discrimination. After 200 ms, there were large scalp ERP and SCD components that demonstrated task related modulations. These effects were identified in the occipital P250 ERP and P250 SCD, plus the superior parietal and superior frontal components of several positive ERP and SCD

peaks between 300-500 ms. These latter scalp components are most likely related to the linguistic encoding and evaluation of attended words.

Furthermore, there were differences in task related component processes between controls and PTSD patients. There were no clear differences in the early sensory detection and discrimination processes, before 200 ms. A possible early stimulus discrimination deficit was demonstrated by a smaller ND250 ERP over posterior temporal regions at 260-290 ms. However, activity at this latency is more likely involved in linguistic encoding and evaluation processes. Clear deficits in PTSD patients were demonstrated by the P450 SCD at superior parietal regions, and the P450/PD400 SCD, and the PD450 ERP components at superior frontal regions. Thus, scalp ERP and SCD components of later stages of selective information processing, from 250-550 ms, indicated abnormal evaluation processes in PTSD.

4.6.2 Stages of Processing

Our understanding of selective attention has come a long way since the seminal works of James (1890). In terms of classical information processing theory (e.g., Neisser, 1967), we consider cognition to consist of several stages, including stimulus detection, encoding, transformation, evaluation and storage (see also Massaro & Cowan, 1993). The effects of attention could modulate activity in any of these stages, but conventional debates refer to early or late selective attention (see, Broadbent, 1970; Treisman & Gelade, 1980; Treisman, 1982, 1996). Early selection generally refers to a filter based on physical stimulus attributes, while later selection may refer to a filter based on object or linguistic stimulus content.

Neuroimaging and ERPs, in particular, offer important evidence for investigating the spatio-temporal dynamics of attention modulations of sensory and perceptual processes. The visual word stimuli of this study provide opportunity for both physical discrimination and also linguistic encoding and evaluation. Although caveats must be

placed on oversimplification of cognitive processes into distinct, discrete stages (see Miller & Hackley, 1992; Massaro & Cowan, 1993), it is useful to at least partially distinguish between elementary visual feature processing and later linguistic encoding and evaluation. ERP components arising before 200 ms are most likely related to early visual feature analysis and perception, rather than linguistic encoding and associative processes, given that word perception requires approximately 150-200 ms (Petersen et al., 1993; Allison et al., 1994; Nobre et al., 1994; Halgren et al., 1994; Kuriki et al., 1998; Schendan et al., 1998; Cohen et al., 2000). The following discussion frames the interpretation of the current findings into these two stages of information processing: (a) stimulus feature discrimination within 150-200 ms and (b) later attended stimulus evaluation.

4.6.3 Visual Feature Processing and Attention

In this study, the first clear indications of occipital visual activity appear at approximately 100-200 ms. The P100 ERP peaked between 90-105 ms over bilateral occipito-temporal regions. There were no attention modulations of this component. This was followed by large occipital negativity, including an N120 SCD at 120-140 ms and an N150 ERP at 140-160 ms. These components demonstrated attention effects, being larger for attended than unattended words. At the same latency, there was a large superior frontal P150 ERP that was also larger for attended words.

This study could not clearly evaluate the early C1 component reported in some studies of selective attention to color. For example, Anllo-Vento et al. (1998) investigated selective attention to color checkerboards and found similar components in both scalp voltage and SCD. There was a negative component over occipital and parietal areas at 70-130 ms (C1), paralleled by a positive component over bilateral inferior occipito-temporal areas at 120 ms (P1). The earlier C1 showed no attention effects, whereas the P1 was larger for attended checkerboards (Anllo-Vento et al.,

1998). Note that results of Anllo-Vento et al. (1998) are derived from thousands of stimulus presentations, with a short inter-stimulus interval and a short baseline period, providing high signal-to-noise measures of the very early visual ERP components, especially the C1. The current study was not specifically designed to measure these early components, having fewer stimuli than the previous work (Anllo-Vento et al., 1998). Also, the C1 component may be related to spatial attributes of their task material (e.g., Foxe & Simpson, 2002), which are not available here. Hence, this study could not clearly identify the C1 component.

The earliest SCD activity of this study was an N80 SCD component that peaked between 80-110 ms over central regions, which was followed by the N120 SCD peak over the occipital area at 120-140 ms. There were no reliable measures of the N80 SCD and no clear indications of any attention effects at that latency. During this time, words appeared for 200 ms, so there must be continuous activity in the visual pathways for 200 ms after stimulus onset. It is likely that the N80 and N120 SCD components arise from early cortical processing in the visual pathways.

The earliest ERP activity was the posterior temporal P100 ERP at 90-105 ms, which demonstrated no attention modulation. This finding is inconsistent with some previous color selective attention studies (Hillyard & Munt, 1984; Wijers et al., 1989a, 1989b, 1989c; Anllo-Vento et al., 1998; Hillyard & Anllo-Vento, 1998; van der Stelt et al., 1998; Valdes-Sosa et al., 1998; Smid et al., 1999). For example, Anllo-Vento et al. (1998) demonstrated a larger P1 for attended checkerboards. This attention effect was clearer in an attention difference component arising over occipito-temporal regions at 130 ms (PD130), with possible sources in extrastriate areas (Anllo-Vento et al., 1998; cf. Corbetta et al. 1990, 1991). There are several possible explanations for this discrepancy. Firstly, the visual checkerboard task stimulates the full visual field, in which colors are easier to discriminate, which would decrease the latency of the

attention modulation (Näätänen, 1990). Secondly, it may be that detection of an attention modulation of the P1 ERP is dependent on spatial aspects of the checkerboard task, which can elicit earlier attention effects in the dorsal visual stream than those reported for activity in the ventral visual stream (e.g., Rao et al., 2003; see also Näätänen, 1990). Also, higher stimulus presentation rates (shorter inter-stimulus intervals) increase the pressure on processing resources to respond quicker, effectively decreasing the latency at which attention modulations are identified (Näätänen, 1990).

The earliest attention effects in this study arise at 120-160 ms over the occipital region, where the N120 SCD was larger for attended words at 120-140 ms and a similar attention effect was identified in the N150 ERP at 140-160 ms. These components are consistent with a similar peak identified by Kellenbach and Michie (1996), which demonstrated larger negative occipital and temporal peaks for attended than unattended words. In the present study, there was an N180 over the posterior temporal area that indicates enhanced activity for the attended words. Thus, early selective attention modulations, related to color discriminations for words, arise in negative scalp ERP and SCD components at 120-180 ms over occipital and temporal regions. These components are related to visual feature analysis and discrimination, involving striate and extrastriate visual cortex.

The frontal P150 ERP demonstrated attention effects at 145-160 ms, which could indicate executive frontal control over early feature selection. This component is similar to a frontal positive component identified by Kellenbach and Michie (1996), although the onset of attention effects is 50 ms earlier here. These frontal attention effects most likely correspond with the FSP of previous work, which has been related to executive attention processes (e.g., Smid et al., 1999). In theory, prefrontal activity indicates executive processes responsible for initiation and maintenance of attention sets, which effectively modulate visual processing in extrastriate areas to create and

maintain a selective bias in the analysis of visual features requiring attention (e.g., Näätänen, 1990; Desimone & Duncan, 1995; Miller & Cohen, 2001). The cortical source(s) of the frontal P150 ERP are not clear, although neuroimaging reports of selective attention to color have found source activity in the anterior cingulate, frontal, and parietal regions (Corbetta et al., 1990, 1991; Petersen et al., 1993; Clark et al., 1997), and passive word presentations can activate frontal semantic systems (Petersen et al., 1990). Also, the timing of the frontal P150 activity accords with studies that indicate activity in frontal and prefrontal cortex within 100-140 ms of visual stimulus onset (Clarke et al., 1995; Nowak & Bullier, 1997; Rainer, Asaad, & Miller, 1998; Foxe & Simpson, 2002). Thus, it is likely that the P150 ERP is an early indication of activity in frontal visual fields and associated executive control of attention.

4.6.4 Visual Processing and Attention in PTSD

The scalp components in this study indicate no significant abnormality of early selective attention in PTSD. Many of the scalp components that arise before 250 ms indicate selective attention effects, based on physical stimulus attributes, but none of those components indicated deficits in PTSD patients. Thus, there are no clear indications in this study of abnormal visual processing and attention to physical stimulus attributes in PTSD.

These findings confirm previous ERP investigations of PTSD, which have often demonstrated normal N1 and P2 ERP components for neutral stimuli (McFarlane et al., 1993; Charles et al., 1995; Metzger et al., 1997; Morgan & Grillon, 1999; Galletly et al., 2001; cf., Felmingham et al., 2002). Note that abnormal P2 amplitude has only been found for auditory stimuli that exceed startle thresholds (Paige et al., 1990) and one study of a conventional oddball task (Felmingham et al., 2002). Together, these findings suggest that auditory and visual sensory processing is not impaired for neutral stimuli in PTSD. However, several recent reports indicate abnormal thalamic gating

(Gillette et al., 1997; Neylan et al., 1999) and a second report indicates abnormal sensory discrimination in PTSD (Morgan & Grillon, 1999).

Neylan et al. (1999) report a sophisticated investigation of P50 habituation for non-startle tones and found less habituation in PTSD patients, which indicates abnormality of sensory gating in thalamic circuits for neutral stimuli (see also Gillette et al., 1997). This evidence is perhaps best explained by abnormality of interactions between thalamic circuits and cortical and limbic systems (e.g., Gray, 1982; Kolb, 1987; Everly, 1989, 1993). In particular, it supports the proposal that trauma leads to hyperarousal or hypersensitivity of sensory systems. If thalamic circuits fail to habituate to neutral stimuli, their cortical projections are overloaded by irrelevant, repetitive information. Kolb (1987) proposed that excessive emotional arousal, especially threat and fear responses of the amygdala, may overload executive systems (e.g., anterior cingulate), leading to less control of subcortical and primary sensory cortical activity, with consequent deficits in cortical discrimination and adaptive response processes (e.g., see Chao & Knight, 1998). Primarily, thalamic nuclei become hypersensitive to any stimulus change, so their projections to the cortex can overload the capacity to process sensory information and impair cortico-thalamic feedback required for effective early discrimination and habituation. Furthermore, a vicious cycle of hyperarousal ensues, as the capacity of cortical processes to regulate brainstem arousal nuclei diminishes. Hence, brainstem arousal centers, such as the reticular system and the locus coeruleus, may escape from cortical control and further enhance the sensitivity of thalamic circuits and their associations with limbic and cortical networks. Neylan et al. (1999) propose that the reduced P50 habituation could be related to deficits in hippocampal functions, which normally inhibit the response of thalamic circuits to repetitive, innocuous stimuli (see hippocampal atrophy literature also, i.e., Bremner et al., 1995, 1997; Gurvitis et al., 1996; Stein et al., 1997). Thus,

there could be abnormal interactions of thalamic circuits and cortical systems in PTSD, resulting in impaired neutral stimulus information processing.

This theory may affect the interpretation of trends toward greater activity in early visual responses for PTSD patients in this study. For example, the occipito-temporal P100 and the N150 ERP appear to have larger amplitude for PTSD patients of this study (see Figure 4-3). Although the statistics indicate that these findings cannot be generalized to a PTSD population, there is a trend for the patient sample of this study toward greater P100 and N150 amplitude, suggesting greater visual cortical activation. These components may usually be interpreted as greater allocation of stimulus processing resources, leading to more effective information processing. However, in this case, the interpretation must take into account whether greater activation is adaptive or efficient. Given the evidence to indicate abnormal stimulus processing in PTSD, it may be more appropriate to interpret these findings in the light of abnormal thalamo-cortical functions. That is, the findings are consistent with decreased habituation of the lateral geniculate and greater cortical activity (e.g., Neylan et al., 1999). Although greater cortical activity might suggest enhanced sensory function in PTSD for neutral stimuli, this is not necessarily the case, as the greater cortical activation might result from abnormal thalamo-cortical interactions, which could indicate (a) dishabituation of thalamic circuits, (b) consequent excess activation of primary sensory cortex, and (c) impaired sensory discrimination.

The explanation becomes more complex when threatening or traumatic information processing is considered. In contrast to the trends identified here for neutral information, Kounios et al. (1997) report diminished P100 over the right posterior temporal region for a series of visual words that contained traumatic and neutral words (the observed effects were not clearly differentiated for traumatic and neutral words). Their results indicate that there are diminished early visual responses for all words in

the presence of traumatic information, whereas the tentative results here suggest enhanced visual activity in the absence of any traumatic stimuli. The findings of Kounios et al. (1997) are also inconsistent with previous reports of enhanced N1 activity for combat pictures (i.e., Attias, Bleich, & Gilat, 1996; Attias, Bleich, Furman, & Zinger, 1996). Thus, their results are difficult to integrate with other findings.

A possible explanation draws on the findings of Paige et al. (1990) for auditory stimuli, whereby these findings could suggest an abnormal sensory gating process, which is biased to avoid traumatic content. To prevent overarousal of the cortical system, PTSD patients may have a systematic bias to greater inhibition of traumatic information, especially within the right hemisphere. However, this interpretation fails in the light of evidence from Attias et al. (1996), which clearly indicates that PTSD patients have enhanced ERP responses to combat images. Thus, the evidence to date is inconclusive on the nature of abnormal early sensory discrimination in differentation of traumatic and/or neutral stimuli. It is only possible to suggest that abnormal thalmo-cortical networks may operate to avoid traumatic or excessive stimulation, with an important trade-off in terms of accurate sensory discrimination for neutral stimuli. It is important to interpret the findings in the light of Kolb's (1987) model and to further model and investigate the variations in information processing for neutral and traumatic content, both simultaneously and separately, perhaps with a view to pharmacological modification of thalamo-cortical networks (although their complex interactions with limbic networks must be accommodated also).

An interesting study of sensory processing in the absence of attention has some important implications for any theory of early sensory processing in PTSD. Morgan and Grillon (1999) investigated early sensory transmission and discrimination in the absence of conscious attention for PTSD patients who suffered sexual assault. They employed an auditory mismatch negativity (MMN) task and found no indications of

abnormal P50, N1 or P2 ERPs, but enhanced N2 amplitude, due to larger MMN activity, in PTSD patients. It must be appreciated that P50 attenuation is very difficult to investigate and the report by Neylan et al. (1999) employed sophisticated analysis procedures to clarify this issue, so that contribution carries greater weight than other studies that are not specifically designed to evaluate the P50. That is, the findings of Morgan and Grillon (1999) on the P50 are less authoritative than those of Neylan et al. (1999)[2]. In any case, Morgan and Grillon (1999) conclude that the P50, N1 and P2 ERPs suggest no abnormality of auditory pathways and cortical processing in PTSD (consistent with previous conscious auditory tasks; McFarlane et al., 1993; Charles et al., 1995; Metzger et al., 1997; Galletly et al., 2001), yet the MMN indicates enhanced activity related to auditory discrimination (Morgan & Grillon, 1999). The MMN is thought to indicate a cortical process for the automatic detection of auditory stimulus changes, involving stimulus registration and comparison in sensory memory, independent of attention (e.g., Näätänen, 1990, part 3). Morgan and Grillon (1999) propose that an increase of the MMN in PTSD indicates enhanced activation of automatic auditory cortex discrimination. That is, the difference in N2 amplitude for target over common auditory stimuli is attributed to greater automatic cortical discrimination. It must be noted that the MMN task is often an easier discrimination task than other auditory tasks used to study PTSD. However, if this result does indicate enhanced automatic cortical processing for sensory discrimination, in the absence of attention, it suggests that previous indications of abnormal sensory discrimination in PTSD may result from abnormal controlled modulation of sensory discrimination

[2] The findings of Morgan & Grillon (1999) require replication. There are several points of concern. Firstly, half of the patient sample had comorbid panic disorder (PD) with agoraphobia. Clark, McFarlane, Weber and Battersby (1996) have demonstrated larger amplitude of P3 in PD and Metzger et al. (1997) report smaller P3 in PTSD patients without PD compared with those with comorbid PD. It is not clear whether similar amplitude trends would be found for the MMN. Secondly, Morgan & Grillon (1999) report that the MMN amplitude is positively associated with PTSD symptoms. As the MMN is a negative component, this means that greater PTSD symptom severity is related to smaller MMN amplitude. Thus, their findings may be confounded by comorbidity.

during conscious attentional processing. That is, the ERP reports of abnormal early sensory discrimination might be confounded by influences from top-down executive systems that modulate sensory discrimination (presumably with the exception of the P50 findings of Neylan et al., 1999).

The findings of the present study do not clearly demonstrate very early sensory discrimination deficits in PTSD, rather they indicate abnormal controlled attention (discussed further below), which, in theory, modulates the automated sensory discriminations indicated by the MMN (see Näätänen, 1990, p. 227). For PTSD patients, it may be possible that deficits of controlled attention fail to effectively control the primary sensory discrimination processes that would be otherwise modulated for more adaptive stimulus discrimination. This could lead to greater variability in ERP responses (e.g., Neylan et al., 2003). These conclusions may be consistent with Kolb's (1987) hypothesis of sensory overload in PTSD, which prevents adequate attention modulation of sensory awareness. In particular, Kolb (1987) hypothesized deficits in sensory discrimination. It may be that automatic, primary sensory discriminations are enhanced by greater cortical activation in PTSD, as indicated by MMN activity (Morgan & Grillon, 1999), while more conscious, controlled attention modulations of these automatic processes fail to have an impact on the heightened activity levels. If so, this may be a reasonable adaptation of Kolb's theory. On the other hand, it may be possible that people susceptible to PTSD have prior executive function deficits that predispose them to excessive sensory activity, especially under stress, leading to excessive novelty detection and associated hypervigilance and hyperarousal, possibly leading to the development and maintenance of PTSD symptoms (see Kimble et al., 2000; see also Näätänen, 1990, part 3). There is an important caveat on this line of argument. That is, active control processes may counter sensory overload under some circumstances, because the capacity for attention modulation of sensation is not entirely

lapse in PTSD, as Paige et al. (1990) provide evidence that excessive stimulation can be inhibited.

4.6.5 Stimulus Evaluation

The stimulus duration of this study was 200 ms, so there is no requirement for working memory representations of the stimuli in this time. However, this does not preclude the requirement to evaluate the current stimulus against a working memory representation of the target attributes.

Clear indications of differential processing of the attended channel arise after 200 ms. The P250 ERP has larger amplitude for unattended than attended words, giving rise to a posterior temporal ND250 ERP at 265-290 ms. This difference component is very similar to the Nd component that is generated by "processing negativity" (Näätänen, 1992). The Nd component is a negative shift in the auditory N1 and P2 ERPs for attended stimuli, which indicates the process of comparing a current stimulus with an attended stimulus template (Näätänen, 1990). The amplitude and duration of this component are related to the similarity of the current stimulus with the attention template. In the visual attention literature, similar components have been referred to as the selection negativity (SN). For example, the SN in Anllo-Vento et al. (1988) arises from greater positive ERP amplitude for unattended than attended checkerboards between 150-400 ms. Also, Kellenbach and Michie (1996) identified a negative attention difference for colored words over posterior temporal and fronto-central regions at 250-450 ms.

Given several assumptions, it is possible to infer that the ND250 ERP indicates the attention modulation and initiation of further processing of visual stimuli. The task demands require, at some point, that processing of the unattended stimulus is inhibited. The precise details of the attention filter may be indeterminate at present (e.g., Näätänen, 1990), although an active inhibition process, controlled by executive

intervention, is most likely (e.g., LaBerge, 1995; Desimone & Duncan, 1995). In any case, it is reasonable to assume that an efficient cognitive system will stop processing information that is identified as irrelevant based on a physical attribute (which is determined within 100-200 ms of stimulus onset). It may be possible to interpret the P250 ERP as an indication of the energy involved in this inhibition process (see Figure 4-4). Furthermore, the occipital ERP waveforms (see Figure 4-5) provide evidence of an important stage in the differential processing of attended vs. unattended stimuli. At 200-400 ms, the P250 ERP has larger amplitude for unattended stimuli, possibly indicating the extra energy generated during inhibition of processing these events (cf. Gevins et al., 1995). There is less amplitude in the scalp components for attended stimuli at this time, suggesting that attended stimuli are less inhibited. Thereafter, the ERP energy for attended events increases, whereas the ERP energy for unattended stimuli decreases. There is a clear switch point at 300-350 ms, suggesting the presence of an effective attention filter and associated differential stimulus processing (see Figure 4-4 & Figure 4-5).

In this study, the ND250 was largest over the left posterior temporal region, consistent with greater left hemisphere linguistic processing (cf. Gevins et al., 1995). The ND250 could arise from modulation of visual processes in the inferior temporal cortex, including color and form processing in lingual and fusiform cortex, and linguistic encoding in lateral posterior temporal cortex (e.g., Gevins et al., 1995; Cohen et al., 2000). The latency of the ND250 suggests that attention modulations in this study occurred after the time required for word form encoding, which occurs within 150-200 ms (Petersen et al., 1993; Allison et al., 1994; Nobre et al., 1994; Halgren et al., 1994; Gevins et al., 1995; Kuriki et al., 1998; Schendan et al., 1998; Cohen et al., 2000). Thus, the ND250 most likely indicates attention modulation of visual form and

linguistic encoding, after the initial selection based on physical attributes alone (color in this case).

Given the initial selection of attended words within 200-300 ms, further processing must indicate evaluation of whether a word is a target, which involves comparison of the current attended word against a target memory. The details of the comparison process are likely to be complex, but an important issue to consider is the nature of the stimulus and target representations. The encoding of visual word stimuli may take several forms, including visual forms (graphemes) and associated transformation into phonemes and semantic representations, with possible activation of multimodal imagery (Gevins et al., 1995).

The most prominent evaluation effects are evident in the P350 and P450 ERP components. In this time frame, the attended words elicit greater positive ERP activity over the parietal and frontal regions. These positive scalp components are similar to components identified by Kellenbach and Michie (1996) and the associated SCD activity in this study demonstrates similar effects over occipito-parietal and left frontal regions. It is likely that the scalp components from 350-500 ms are indications of the evaluation of attended non-target words, which precedes target response execution. The parietal and frontal activity could arise from executive association modules in a distributed, reciprocal associative network, including areas of frontal and parietal cortices, which have been demonstrated in brain imaging studies of attention and working memory (e.g., Posner & Raichle, 1994; Clark et al., 2000; Clark et al., 2001).

The parietal components of this study and that of Kellenbach and Michie (1996) persist longer than similar visual attention components for letters, numbers and checkerboards (Wijers et al., 1989a, 1989b, 1989c; Anllo-Vento et al., 1998; Hillyard & Anllo-Vento, 1998; van der Stelt et al., 1998; Valdes-Sosa et al., 1998; Smid et al., 1999). The parietal components of previous studies dissipate after 350 ms; whereas

those in the present study persist from approximately 300-600 ms (see also Kellenbach & Michie, 1996). A possible explanation for these differences may lie in different stimulus presentation rates, with faster rates leaving less time available for stimulus evaluation processes. An alternative or additional explanation relates to the nature of the stimuli. The previous color attention studies present geometric or single letter or number stimuli, which are not readily assimilated into elaborate semantic or episodic associative memory networks. The word stimuli of this study offer the opportunity for more elaborate, extended semantic processing. The persistence of the activity in the present study may indicate associative linguistic encoding processes, which involve controlled working memory manipulations of stimulus representations and transformations. The topography of the activity in this study suggests involvement of a distributed network, including frontal and parietal associative processes. The duration of the evaluation components in the present study suggest that the linguistic task stimuli elicit elaborate, semantic encoding and evaluation.

The ERP literature has identified stimulus evaluation processing with potentials occurring at approximately 300-400 ms, including the P300 ERP. It is well documented that a large positive ERP arises over parietal regions during rare or novel stimulus evaluation (McCarthy & Donchin, 1981; Johnson, 1988). It is not so well documented in relation to non-target stimuli. The P350 and P450 ERPs of this task have similar topography to the conventional oddball P300, yet they are elicited by non-target words. The amplitude of these components may be smaller than that of the target ERPs, as these non-target stimuli require no overt response (no responses were made to any of the trials comprising the averaged ERPs presented here, so these ERPs cannot indicate response execution processes). It is interesting to note that the PD450 ERP amplitude was negatively related to target reaction time; with decreases in PD450 amplitude, target reaction time increased. Thus, the activity at this time is associated with target

detection processing. It is most likely that these scalp components are related to stimulus evaluation processing that precedes target detection and thereby determines response latency and accuracy. Similar relationships between target P300 and response time have been documented (McCarthy & Donchin, 1981; Magliero et al., 1984). If these non-target ERPs are at all directly related to response processes, it is most likely the preparation and withholding of responses to the stimuli once identified as non-target events.

In theory, very fast target detection may be achieved when the target information is represented and remembered as a primary visual experience. This might allow more immediate, visual template evaluations of the current stimulus event. This could be processed in working memory, including activation of the visuo-spatial scratchpad (Baddeley, 1992). The sources of the visuo-spatial scratchpad may involve visual perceptual functions instantiated in the occipital and parietal cortices. In this study, the topography of the later evaluation components appears to implicate parietal and frontal regions, rather than occipital regions. While this conclusion is tentative, the findings do suggest that evaluation processing has involved a transformation of any visual perceptual encoding into elaborate phonological and possibly semantic associative representations.

A possible phonological encoding of the stimulus information is suggested by P400 activity in the left frontal region. Extensive research on working memory processes illustrates that working memory can involve an internal, controlled phonological rehearsal (the phonological loop; Baddeley, 1992). The task presented linguistic information that can be phonologically encoded. It is possible that the frontal components of the P400 indicate the internal generation and rehearsal of phonological information. Moreover, the attended stimuli elicit greater amplitude in this region than

unattended stimuli, which suggests that target detection involves greater phonological processing of the attended stimulus.

4.6.6 Stimulus Evaluation in PTSD

Several group differences were apparent in components arising after 250 ms. These effects were demonstrated by the posterior temporal ND250 ERP and later frontal PD450 ERP/SCD components.

The posterior temporal ND250 ERP was larger in controls than PTSD patients. This group difference appeared to be largely due to a smaller P250 ERP in patients than controls for the unattended words (see Figure 4-4), although this difference was not significant. The ND250 amplitude was linearly related to both trait anxiety and depression; it became larger with increasing trait anxiety, but smaller with increasing depression. Also, for patients, there was a negative relationship between ND250 latency and CAPS criterion C; it arose earlier as symptoms of avoidance and withdrawal increased. These findings indicate an abnormality of the controlled attention modulation of sensory processing in PTSD patients.

Previous ERP studies of PTSD have found abnormalities of N2 ERPs for rare distracters or targets (e.g., McFarlane et al., 1993; Galletly et al., 2001; Felmingham et al., 2002). These findings have been interpreted as an indication of difficulty with stimulus discrimination. The present study extends these findings to visual processing of neutral common stimuli. This finding suggests that controlled attention to even neutral common stimuli may play an important role in patient's concentration difficulties.

Note that the ND250 of this study is smaller in PTSD, whereas the MMN is larger in PTSD (Morgan & Grillon, 1999). These components do arise at similar latencies and from similar attention effects, but there are important differences between them. One difference is that this study is a visual task that does not elicit the MMN, which is

derived from auditory stimulus trains (Näätänen, 1990). A more important difference is that the MMN is generated by automatic cortical discrimination processes, which automatically detect rare changes in pitch among a series of tones, even in the absence of attention to the tones (Näätänen, 1990), whereas the ND250 is related to conscious, controlled attention modulation of sensory processing. As explained above, these differences in automatic and controlled processing may be the key to understanding these findings for PTSD patients.

It may be possible to interpret the ND250 as an indication of executive intervention to inhibit unattended stimuli. If this is the case, it suggests that PTSD patients are failing to inhibit the processing of irrelevant stimuli. This may be consistent with Kolb's (1987) theory of excessive cortical arousal in PTSD, as discussed above. It is interesting to note that the latency of the ND250 peak decreases with greater symptoms of avoidance and numbing (cf., decreases in target P3 with numbing, Felmingham et al., 2002). It may be possible to interpret this trend as an indication of greater effort to control stimulus overload for some patients (e.g., Paige et al., 1990). It is not clear, however, whether this effort may effectively decrease stimulus discrimination time without any consequent lapse in accuracy.

The attention effects in the frontal P400 ERP and the frontal and parietal P450 SCD were demonstrated for controls, but not PTSD patients. These attention effects were related to the PD450 ERP/SCD over frontal regions at 440-480 ms, which were also larger for controls than PTSD patients. The PD450 ERP amplitude was negatively related to trait anxiety and depression; as these symptoms increased, the amplitude of the PD450 ERP decreased (with associated increases in reaction time, see above).

These findings bear important similarities with previous findings of deficits in P3 activity in PTSD (McFarlane et al., 1993; Charles et al., 1995; Metzger et al., 1997; Kimble et al., 2000; Galletly et al., 2001; Felmingham et al., 2002). The previous P3

findings for infrequent target or distracter stimuli suggest impairment of stimulus evaluation and context updating (e.g., Donchin & Coles, 1988). This study confirms that the P3 effects identified previously are related to stimulus evaluation, although for frequent events that do not startle or indicate any degree of novelty or threat. That is, this study has identified impairment in stimulus evaluation for non-target events, which is associated with response time (see above).

The topography of the current ERP findings suggests deficits in activity at frontal regions. Although there are clear indications of parietal activity involved in stimulus evaluation processing, the group differences are identified in frontal ERPs in this study, which is inconsistent with some previous findings of parietal P3 ERP deficits (McFarlane et al., 1993; Charles et al., 1995; Metzger et al., 1997; Felmingham et al., 2002). There is evidence of dissociations between frontal P3a and parietal P3b components for infrequent stimuli, with P3a indicating an orienting response, while P3b indicates further stimulus evaluation (e.g., Nielsen-Bohlman & Knight, 1999; see also Halgren & Marinkovic, 1995; Daffner et al., 2000). It is not clear, however, whether these distinctions can be applied to the present findings, as the stimuli of this study do not conform to conventional novel stimuli that elicit a P3a response (cf., Kimble et al., 2000). Furthermore, the SCD analyses of the present study indicate deficits in PTSD over both the frontal and parietal regions. Given these results, it is possible that the current findings indicate deficits in frontal and parietal executive activity that form part of a larger distributed network of associative processes engaged in stimulus evaluation.

Abnormalities of discrimination and evaluation processing in PTSD are the antecedents of poor performance, including decreased target detection accuracy and delayed target detection. In this study, patients demonstrated large early visual responses to both attended and unattended words. However, the scalp components indicate that they do not clearly distinguish between relevant and irrelevant information.

This discrimination process, given adequate visual cortical responses to stimuli, depends on accurate contextual evaluation, which is known to depend on septo-hippocampal and associative, executive functions (Gray, 1982). In the absence of adequate contextual evaluation, target detection criteria become less stringent, to make allowance for evaluation ambiguity and thereby enable successful target detection, but at the cost of accuracy (i.e., false positives). Thus, PTSD patients demonstrate deficits in early visual discrimination and/or contextual evaluation that can lead to misdirected or delayed actions.

4.6.7 Conclusions

4.6.7.1 Components of Stimulus Selection and Evaluation

In this study, several stages of visual stimulus selection and evaluation were demonstrated with electrophysiology. Early occipital scalp potentials demonstrated attention modulations, suggesting some degree of early discrimination or filtering of attended stimulus features at 120-160 ms. A positive frontal scalp potential at this time also demonstrated attention modulation, suggesting involvement of frontal executive systems in the maintenance of an attention channel. After 200-250 ms, there were clear indications of differential processing for the attended words, involving posterior temporal, parietal and frontal regions. A large negative difference component over posterior temporal regions at 250 ms indicated the selection of attended stimuli for further processing. This activity may have involved extrastriate areas of the ventral visual processing stream in stimulus feature integration and object selection. Further processing of the attended stimuli involved linguistic encoding and stimulus evaluation processes, which are related to response time and accuracy of target detection. There were large positive components over parietal and frontal regions at 300-600 ms, which

suggested involvement of a distributed executive system in the evaluation of attended stimuli.

4.6.7.2 Stimulus Selection and Evaluation in PTSD

The findings of this study, together with previous work, clearly indicate that PTSD involves a disturbance of neutral information processing. The current findings provide evidence of a dysfunction of controlled attention for neutral linguistic information. Although a couple of previous studies have identified deficits of automatic thalamic and early cortical attention processes, there were no indications of such deficits in the present study, which involved an active, controlled attention task. Rather, this study implicates deficits in the controlled modulation of sensory discrimination and selection, largely indicated by decreased amplitude of the ND250 ERP, which supports some previous findings of abnormal N2 ERPs. Furthermore, this work indicates deficits in PTSD patients for non-target stimulus evaluation during a target detection task. All previous ERP findings of deficits in PTSD for neutral information are related to rare target or distracter stimuli. The findings of this study provide a clear indication, for the first time, of non-target stimulus processing deficits in PTSD, which are not related to stimulus novelty. The implications of this finding are that PTSD patients have very general deficits in neutral stimulus information processing. Furthermore, this work has demonstrated that these deficits are associated with clinical symptoms, including anxiety and avoidance symptoms. These deficits in stimulus selection and evaluation in PTSD could explain increased uncertainty and anxiety, associated with hypervigilance and sensitivity to novel distraction. A potential explanation for these deficits draws on Kolb's (1987) neuropsychology model and recent work on hippocampal functions and associated episodic memory processes.

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