Electrophysiology of Combat-Related PTSD

JOHN KOUNIOS,[a,c] BRETT LITZ,[b]
DANNY KALOUPEK,[b] DAVID RIGGS,[b] JEFF KNIGHT,[b]
FRANK WEATHERS,[b] JANE E. ANDERSON,[b] AND
TERENCE KEANE[b]

[a]*Department of Psychology*
University of Pennsylvania
3815 Walnut St.
Philadelphia, Pennsylvania 19104–6196

[b]*National Center for PTSD*
Boston Veterans Affairs Medical Center (116B-2)
150 S. Huntington Ave.
Boston, Massachusetts 02130

One technique that has been applied to the study of posttraumatic stress disorder (PTSD) is the measurement of event-related brain potentials (ERPs).[1] ERPs are measured by scalp-electrode recordings of a subject's electroencephalogram during performance of a task involving discrete stimulus and/or response events. Segments of the electroencephalogram following presentations of members of a class of stimuli are averaged, yielding a wave depicting the brain's average electrical response to that stimulus class. Analyzing the temporal information given by the positive and negative deflections of such a wave and the spatial information provided by an array of electrodes distributed across the scalp yields valuable neurophysiological and functional-anatomical information.[2]

We explored the neurophysiology of PTSD by measuring ERPs while patients and control subjects viewed threatening and relatively nonthreatening words. In particular, we examined differences between patients and controls that could elucidate whether PTSD is best characterized as an exaggerated neural response specifically to trauma-related stimuli or a general disorder characterized by aberrant brain responses to all stimuli.

Sixteen male, right-handed, native English-speaking, Vietnam-era combat veterans participated. Eight were diagnosed with PTSD; the others were well-adjusted veterans (WAV). ERPs were measured with 64 tin electrodes mounted in an elastic cap (referenced to the left mastoid). The stimuli were a sequence of words displayed on a monitor. There were three blocks of words, each consisting of 45 "trauma" words (related to combat experiences in Vietnam, e.g., grenade), 45 comparatively neutral "nontrauma" words (related to school experiences, e.g., pencil), and 18

---

[c] Address for correspondence: John Kounios, Ph.D., Department of Psychology, University of Pennsylvania, 3815 Walnut St., Philadelphia, PA 19104-6196 (tel: (215)573-5767; e-mail: jkounios @cattell.psych.upenn.edu).

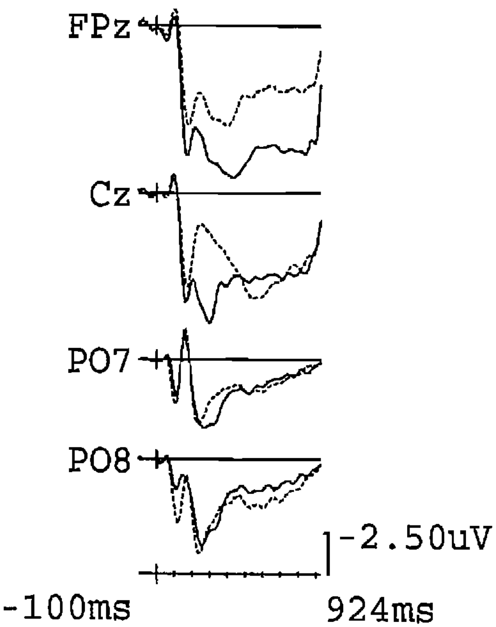

FIGURE 1. Event-related brain potentials (ERPs) for PTSD and WAV subjects averaged across blocks and stimulus types (with negative voltages plotted up; time from left to right; PTSD ERPs as *solid lines;* WAVs as *dashed lines.*

infrequent target food words (e.g., bread), all intermixed in random order. The three blocks used the same trauma and neutral words intermixed with new food words (in a new random order).

Subjects fixated at a "+" sign at the center of the screen. On each trial, this fixation mark was replaced by a word for 2,000 ms. This was followed by the reinstatement of the fixation mark for 2,000 ms. followed by the next word, etc. Their task was to press a button with the index finger of their right hand whenever the displayed word was a type of food and to do nothing if the word was not a food.

Subjects' EEG's were amplified (50,000×), digitized at 250 Hz, and recorded continuously. ERPs were computed by averaging (separately for each block and type of stimulus) 1,048-ms segments of artifact-free EEG beginning 100 ms prior to stimulus onset. The results reported focus on major differences between the ERPs of PTSD and WAV participants in response to the trauma and nontrauma stimuli.

One finding concerns an early positive deflection in the ERP peaking at 120 ms (i.e., P1) and focused bilaterally over left (PO7) and right (PO8) parietooccipital electrode sites. FIGURE 1 shows this deflection averaged across blocks and stimulus types (with negative voltages plotted up; time from left to right; PTSD ERPs as solid lines, WAVs as dashed). Although the amplitude of this component was not reliably influenced by repetition or stimulus types, there was a clear difference between the PTSD patients and WAVs. Specifically, P1 amplitude did not differ reliably across groups over the left posterior cortex (site PO7), but it was diminished over the homologous right hemisphere area (PO8) for the PTSD patients relative to the WAVs.

P1 has been the focus of studies of attention in normal subjects which suggest that this wave is generated in ventrolateral extrastriate cortex (probably the fusiform gyrus) and is associated with a gain-control mechanism that regulates the amount of visual information passed along to inferotemporal cortex.[3] Accordingly, the present finding suggests that visual information transmission to inferotemporal cortical centers responsible for higher visual function is attenuated in PTSD patients, but only in the right hemisphere.

A second finding is of a difference in the ERPs measured over prefrontal cortex. As FIGURE 1 shows, the prefrontal ERPs (at midline site Fpz) of PTSD patients were shifted to the positive relative to those of the WAV controls (with no significant difference between trauma and nontrauma stimuli). Such slow, tonic, DC-like shifts have become a focus of interest in recent years and are thought to reflect changes in the firing thresholds of large-scale neuronal networks. In particular, some evidence suggests that such positive shifts may reflect neuronal hyperpolarization (i.e., reduced excitability), whereas negative shifts represent neuronal depolarization (i.e., increased excitability).[4] Such results are important to the study of PTSD, because prefrontal cortex has been implicated in the control, suppression, and coordination of emotion (e.g., via inhibitory inputs to limbic and temporal areas), and because prefrontal deficiency has been suggested as playing a role in PTSD.[5]

This study also revealed a striking brain response in the 250-350-ms time window. As FIGURE 1 shows, subjects with PTSD yielded a distinct positive peak circa 300 ms ("P300tr") in the ERP where the WAV participants yielded a negative trough. This peak was broadly distributed, with a maximum near vertex site Cz. There were no consistent stimulus effects in this time window. Previous ERP studies of emotion in normal subjects found (and mislabeled) positive deflections in this time window, although these studies all found larger deflections for emotional stimuli than for neutral stimuli.[6] This result suggests that the PTSD subjects were reacting strongly to all the words, irrespective of their associations with traumatic experiences, whereas the WAVs were reacting weakly to all the words, irrespective of their associations. This suggests that PTSD can be characterized by a heightened neurophysiological response to all such stimuli, at least in a context in which threat-related stimuli appear frequently, and that WAVs, despite their traumatic experiences, do not have PTSD because (at least in such threatening situations) they can suppress this response to all stimuli.

These results demonstrate three abnormalities associated with PTSD. First, the attentuated right-hemisphere P1 suggests an adaptive strategy to limit perceptual input to downstream processors in the same hemisphere (which is known to play a special role in emotional processing and autonomic arousal). Second, the positive shift at prefrontal sites indicates a different tonic level of cortical excitability over an area of the brain known to be involved in the suppression and control of emotion. And third, the newly identified P300tr component suggests an exaggerated emotional response by PTSD patients. Conversely, this P300tr was suppressed to all stimuli in WAV subjects. This suggests that future studies of the neurophysiology of PTSD examine the responses of individuals who have had traumatic experiences but do not have PTSD. Such individuals may also be "abnormal," albeit in an adaptive fashion that permits them to escape the consequences of emotional trauma.

REFERENCES

1. (a) PAIGE, S. R., G. M. REID, M. G. ALLEN & J. E. O. NEWTON 1990. Psychophysiological correlates of posttraumatic stress disorder in Vietnam veterans. Biol. Psychiatry **27:** 419-430.
    (b) MCFARLANE, A. C., D. L. WEBER & C. R. CLARK. 1993. Abnormal stimulus processing in posttraumatic stress disorder. Biol. Psychiatry **34:** 311-320.
    (c) CHARLES, G., M. HANSENNE, M. ANSEAU, W. PITCHOT, R. MACHOWSKI, M. SCHITTECATTE & J. WILMOTTE. 1995. P300 in posttraumatic stress disorder. Neuropsychobiology **32:** 72-74.
2. HILLYARD, S. A. & T. W. PICTON. 1987. Electrophysiology of cognition. *In* Handbook of Physiology: Section 1. Neurophysiology. F. Plum, Ed.: 519-584. American Physiological Society. New York.
3. (a) MANGUN, G. R., S. A. HILLYARD & S. A. LUCK. 1993. Electrocortical substrates of visual selective attention. *In* Attention and Performance XIV. D. E. Meyer & S. Kornblum, Eds.: 219-243. The MIT. Cambridge, MA.
    (b) HEINZE, H. J., G. R. MANGUN, W. BURCHERT, H. HINRICHS, M. SCHOLZ, T. F. MUENTE, A. GOES, M. SCHERG, S. JOHANNES, H. HUNDESHAGEN, M. S. GAZZANIGA & S. A. HILLYARD. 1994. Combined spatial and temporal imaging of brain activity during visual selective attention in humans. Nature **372:** 543-546.
4. MCCALLUM, W. C. & S. H. CURRY (Eds.). 1993. Slow Potential Changes in the Human Brain. Plenum. New York.
5. (a) DAVIDSON, R. J. & S. K. SUTTON. 1995. Affective neuroscience: The emergence of a discipline. Curr. Opin. Neurobiol. **5:** 217-224.
    (b) LE DOUX, J. E. 1994. Emotion, memory, and the brain. Sci. Am. **270:** 50-57.
6. (a) STORMARK, K. M., H. NORDBY & K. HUGDAHL. 1995. Attentional shifts to emotionally charged cues: Behavioral and ERP data. Cognit. Emotion **9:** 507-523.
    (b) JOHNSTON, V. S., M. H. BURLESON & D. R. MILLER. 1987. Emotional value and late positive components of ERPs. *In* Current Trends in Event-Related Potential Research. R. Johnson, Jr., J. W. Rohrbaugh & R. Parasuraman, Eds.: 198-203. Elsevier. Amsterdam.
    (c) YEE, C. M. & G. A. MILLER. 1987. Affective valence and information processing. *In* Current Trends in Event-Related Potential Research. R. Johnson, Jr., J. W. Rohrbaugh & R. Parasuraman, Eds.: 300-307. Elsevier. Amstersdam.