

N88 - 23388

5/8-53

THE N2-P3 COMPLEX OF THE EVOKED POTENTIAL
AND HUMAN PERFORMANCE

140806
188.

Brian F. O'Donnell and Ronald A. Cohen
Department of Neurology
University of Massachusetts Medical School
Worcester, MA

MK

170541
C-4

When sensory receptors are stimulated, a series of negative and positive deflections time-locked to stimulus onset may be evoked in the electroencephalogram (EEG). Since these potentials are evoked by sensory stimulation, they are called sensory-evoked potentials (EPs). Because of the small magnitude of the EP in relation to ongoing background noise, many stimulus trials must be averaged to obtain a stable EP.

EP waveforms are quantitatively characterized in terms of components. Unfortunately, there is no consensus in the field as to the formal definition of a component (ref. 1). For the paradigms discussed in this paper, components are identified with specific positive and negative deflections in the averaged EP. The deflections are labeled by their polarity and order of appearance. Polarity of a deflection is either positive or negative, denoted by the prefixes "P" or "N". N1, for example, would be the first major negative deflection observed after presentation of an auditory stimulus. N1 generally occurs about 100 milliseconds (ms) after stimulus onset, and is for this reason sometimes labeled N10). Labeling components by their polarity and latency after stimulus onset ("N100", "P300") is another frequently used convention in the EP literature.

EP components are functionally categorized into two types, exogenous and endogenous. Exogenous components of the EP are primarily responsive to properties of the stimulus, such as duration, intensity, and frequency. Typically, exogenous components have short latencies (less than 100 ms after stimulus onset). They usually originate from the primary sensory pathways and projection areas. The morphology and scalp distribution of exogenous components vary greatly between stimulus modalities, and are relatively little affected by task demands.

Endogenous components of the EP vary with psychological factors such as task relevance, expectancies, and task difficulty. EPs associated with endogenous components are frequently referred to as event-related potentials (ERPs). In this paper, the properties of a set of endogenous components, the P3 complex, will be discussed. The P3, or P300, component has received continued experimental attention since it was first reported by Sutton, Braren, Tueting, Zubin and John (refs. 2 and 3). The P3 is a long latency, endogenous component of the evoked potential which can be elicited by auditory, visual, or somatosensory stimuli. In a typical paradigm, the P3 is evoked when a subject attends to rare target tones among a train of more frequently presented non-target tones. P3 usually appears at a latency between 250 and 800 ms after stimulus onset. It is generally preceded by a negative deflection (N2) and followed by a deflection whose polarity varies with scalp topography, the "Slow Wave" (ref. 4). These endogenous

C-4

components are shown in Figure 1. While N2 and P3 usually appear sequentially, they are dissociable. The topography of N2 is modality specific; that is, its peak amplitude appears at different locations on the scalp depending on modality of stimulation (refs. 5 and 6). P3 shows a modality non-specific scalp topography, with peak amplitude over the parietal area of the scalp. N2 appears to a stimulus mismatch whether or not the stimulus is task relevant, whereas the P3 response is attenuated or absent under these conditions (ref. 7). The neural generators of P3 are not known with any specificity. Evidence from depth electrode recordings and correlations with magnetic fields suggest that medial temporal lobe and frontal lobe structures may be involved (refs. 8 to 10).

This paper will address the responsivity of the N2 and P3 components of the EP (the N2-P3 complex) to factors modulating human performance. The first section reviews experimental factors and paradigms. The second and third sections examine the effects of brain dysfunction and pharmacological manipulations on the N2-P3 complex. The functional significance of the N2-P3 complex and its utility as a tool for probing human performance will then be discussed.

Factors Which Influence the N2-P3 Complex

Probability and Task Relevance

Variations in stimulus probability are associated with changes in N2-P3 amplitude (ref. 2). The effect of probability on P3 amplitude is enhanced when the stimuli are task relevant (ref. 11). When a stimulus is ignored, the P3 deflection that occurs (P3a) may represent a different component from the P3 deflection to a task-relevant stimulus (P3b) (ref. 4). A large P3 may be evoked without task demands when a rare tone is very disparate in intensity and frequency from a frequent tone (ref. 12). Task relevant stimuli are usually associated with N2-P3 activity even when the stimuli are equiprobable in relation to the irrelevant stimuli (ref. 2). N2 amplitude is less sensitive to task demands, suggesting that it may represent an automatic match-mismatch detection process (ref. 7). The amplitude of P3 is inversely related to stimulus probability, approximating its information content as defined by classical information theory ($-\log_2 p$) (ref. 13). P3 amplitude to a feedback signal regarding a previous judgment on a target detection task is related to the joint probability of the initial stimulus and the subject's response, termed outcome probability (ref. 14) or contingent probability (ref. 13).

Sequential stimulus structure also contributes to N2-P3 amplitude. The first stimulus of a series elicits a N2-P3 complex. A tone preceded by one or more of the same tones shows diminished N2-P3 amplitude, and one preceded by a series of differing tones shows larger amplitude responses (ref. 15). K. Squires et al. (ref. 15) used a linear additive model defining expectancy as a combination of decaying memory for events, structure sequence, and global probability for up to fifth order stimulus sequences. The model accounted for 78% of the variance of N2-P3 amplitude. Duncan-Johnson and Donchin (ref. 11) similarly found that global probability and sequential structure had independent effects on the P3 complex.

In summary, global stimulus probability and stimulus sequence are

important determinants of the amplitude of the N2-P3 complex. These effects interact with the task-relevance of the stimulus. Task relevant stimuli produce a N2-P3 complex, and the effect of probability is greatly enhanced when stimuli are task-relevant. The joint effects of task relevance and probability provide an example of the sensitivity of electrophysiological measures to aspects of information processing and attentional reactivity not readily apparent from traditional psychological paradigms.

Orienting response

Both N2 and P3 have been associated with the orienting response (refs. 7, 16 and 17). The orienting response is elicited by a variation in stimulus properties, presumably because of a mismatch between the previous representation of the stimulus and the physical properties of the current stimulus. The response is manifested by a range of autonomic, somatic, and EEG changes (ref. 17). The N2-P3 complex fits this model in its reactivity to stimulus change and probability. It diverges from the classical orientation response in its resistance to habituation, even over prolonged periods of time (refs. 18 and 19). One difficulty in making comparisons between the N2-P3 complex and the orienting response is that few studies have used both autonomic and EP measures simultaneously in classical orienting paradigms. A second difficulty is that experiments designed to elicit the N2-P3 complex use short inter-stimulus intervals and task relevant stimuli, while the orienting response classically has not been associated with explicit task demands (ref. 20). A recent study by Rosler (ref. 21) compared N2, P3, skin conductance and HR to rare and frequent visual stimuli. The results indicated that these different response modalities were related to different aspects of task demands and stimulus properties. Rosler concluded the ensemble of autonomic and EP measures was not part of a single orienting reflex, but rather was sensitive to different stages of information processing. Late negative waves occurring after the N2-P3 complex (Slow Wave, "O" wave, CNV) have been argued to be more closely related to the orienting response (ref. 17 and 22).

N2-P3 and motor response

N2 latency, P3 latency, and reaction time (RT) tend to be correlated, particularly when accuracy of response is stressed over speed of response (ref. 23). The P3 component, however, occurs too late after stimulus onset to be concurrent with stimulus discrimination and a precondition for response selection and execution. Ritter and colleagues (ref. 24) have argued that N2 is a better time marker for stimulus discrimination. Goodin and colleagues (ref. 25), however, report data (using EMG onset as a measure of reaction time) which suggest that N2 may also be too late in time to directly index stimulus discrimination. It is possible that the processes represented by N2 and P3, as well as response selection, are initiated in parallel by early stimulus analysis, but the response selection is not necessarily contingent upon N2-P3 related activities in the nervous system. A recent experiment by Goodin and colleagues (ref. 26) demonstrated that P3 and an earlier endogenous component, P165 (Figure 1), were synchronized with both stimulus appearance and response onset as measured by EMG activity, while N2 was more synchronized with stimulus onset than response onset. These results provide further evidence that N2 may represent an independent process from P3, even though they appear sequentially in the averaged EP.

Stimulus evaluation and signal detection

Stimulus evaluation. Stimulus intensity is inversely related to P3 latency (ref. 27). Increased difficulty of discrimination is associated with increased N2 and P3 latency (refs. 28 to 32). Task demands which increase the complexity of stimulus evaluation increase P3 latency and RT, while task demands which increase the difficulty of response selection increase RT latency without affecting P3 latency (ref. 32). Variations in visual stimulus intensity, contrast, and complexity have additive effects on P3 latency (ref. 31). These results have led several investigators to propose that P3 latency provides an index of stimulus discrimination in the nervous system (refs. 23 and 29). Because RT is not temporally contingent on P3, however, it appears more likely that P3 latency represents further processing of a stimulus contingent on initial discrimination, and parallel to response selection.

Signal detection. The effects of observer sensitivity and decision confidence on P3 latency have been studied by a number of investigators. N1 has been related to quantity of signal information received by the subject, while P3 characteristics reflect decision confidence (ref. 33). P3 amplitude increases, and latency decreases, with increasing confidence for correct detection (Hit) of a signal (refs. 34 to 36). In general, false alarms, misses, and correct rejections in signal detection tasks are associated with smaller amplitude P3s. P3 responses will occur to confident false alarms (ref. 33). Correct rejections generate P3s only when signals are highly detectable and signal-absent trials are rare (ref. 35). When signals are of low detectability, probability of presentation has little effect on P3 amplitude (refs. 34 and 35). In a study of signal detection and recognition, P3 amplitude increased and latency decreased as a function of both signal detection and recognition, while N1 only varied with signal detection (ref. 36).

In summary, while P3 probably does not provide a direct marker for the time of stimulus discrimination in the nervous system, it does provide a sensitive measure of the process of stimulus evaluation. P3 latency increases with difficulty of a discrimination. P3 amplitude, on the other hand, reflects decision confidence related to both detection and recognition of signal. The N2-P3 complex in conjunction with RT provides a powerful paradigm for the chronometric analysis of stimulus processing, decision processes and response generation in the human central nervous system (CNS).

Mental load

The findings that the amplitude of P3 was modulated by task relevance and attentional focus, and signal its latency to stimulus evaluation led investigators to link P3 amplitude to the conscious deployment of limited capacity processing resources (refs. 37 and 38). Several lines of research are consistent with this formulation, and suggest that P3 is sensitive to the mental load presented by a task.

The Stroop interference effect, which appears to be due to response interference, prolongs RT without affecting P3 latency (ref. 39). Dual task performance diminishes P3 amplitude on the primary task when the secondary task makes demands on perceptual resources, though not when further demands

are placed on elaboration of a response. RT is responsive to both types of demands (refs. 40 and 41). Wickens and colleagues (ref. 38) hypothesized that if processing resources allocated to a primary and secondary task were reciprocal, this relationship should be reflected in variations in P3 amplitude to stimuli in both tasks. Using visual tracking as the primary task, and an auditory oddball sequence as the secondary task, they compared P3 amplitude to stimuli within each task. As the resource demands of the primary task were increased, P3 amplitude evoked by primary task events increased, whereas those elicited by the auditory stimuli used in the secondary task decreased. A distinction between the responsivity of N2 and P3 amplitude to task relevant and irrelevant workload was reported by Horst and colleagues (ref. 42). When subjects were required to monitor multiple visual readouts, increasing workload was associated with increased negativity in the N2 region of the waveform, regardless of whether the readout was currently task relevant. In the P3 regions of the EP, however, increased workload only affected component amplitude to attended, task-relevant stimuli.

Automatic and controlled processing in visual search tasks (ref. 43) have also been investigated using EP and RT paradigms. N2-P3 amplitude was comparable in automatic and controlled tasks in two studies, while both P3 and RT latencies were shortened in the automatic task (refs. 44 and 45). Memory set size did have an effect on amplitudes, however: N2 amplitude was smaller, and P3 amplitude larger, with increased memory set size (ref. 45). These results suggest that practicing a controlled mapping task (comparing a stimulus to a constant set of items in memory) may reduce the slope of stimulus evaluation and reaction time on memory set size to zero, but the task still requires perceptual resources for performance.

These initial studies suggest that P3 amplitude reflects the mental demands on limited-capacity perceptual resources. In conjunction with RT measures, it may provide a means of differentiating perceptual and response related resource demands involved in performance of specific tasks.

Learning and Memory

P3 amplitude is enhanced to stimuli which are examples of an infrequently occurring category in a series when the stimuli share no common physical properties (refs. 23 and 46). Such results suggest that learned categories in long term memory can be probed by N2-P3 responsivity. The learning process has been experimentally investigated by requiring a subject to learn, either intentionally or not, a set of items, and then measuring the magnitude and latency of P3 of items correctly recognized or missed on a subsequent exposure. P3s to recognized stimuli were larger in amplitude and shorter in latency than those to unrecognized stimuli or distractors, independent of relative probabilities. These results were interpreted to be consistent with the hypothesis that recognized items are more familiar, hence more discriminable, than unrecognized items (refs. 47 and 48). On repeated learning tests, P3 latency becomes shorter and P3 amplitude larger for correctly identified targets (ref. 48).

Several studies have examined whether P3 amplitude or latency to a stimulus on initial exposure predicts subsequent recognition performance. The hypothesis advanced by Donchin (ref. 49) that P3 reflects the process of context or schema updating suggests that stimuli associated with enhanced P3

activity should be more memorable than those that are not. Tests of this hypothesis have not led to consistent results. Sanquist et al. (ref. 47) reported an apparent (but statistically untested) increased amplitude during semantic processing of items which were later recognized. Fabiani, Karis and colleagues (refs. 50 and 51) reported a similar effect, but only when the subjects used a rote rehearsal strategy, or no strategy at all, in the process of learning the material; elaborative strategies produced no P3 enhancement. P3 latency, but not amplitude, on repeated exposures of a list was shorter for words later recognized than to those that were not recognized. This effect may have been due to increased familiarity and discriminability of recognized words over repeated trials. In a continuous recognition task, P3 amplitude on initial exposure has been found to be predictive of later correct recognition (ref. 52). These results suggest that the latency or amplitude of P3 response may predict later recognition performance, although the nature and strength of this effect may be paradigm specific.

Brain Dysfunction and the N2-P3 Complex

The N2-P3 complex has been studied in relation to normal aging, in psychopathology, and in neurological brain disorders. The most intensively studied clinical populations include patients with dementing disorders, schizophrenia, and depression. Variations of oddball paradigms, without or without RT measures, have been the most frequently used EP tests. The P3 component has been the most generally measured EP component in these disorders, although some studies also report characteristics of other components.

Aging

After adolescence, N2 and P3 latency show a continuous increase in latency. The rate of prolongation is about 1 to 2 ms per year. A decrease in P3 amplitude has also been reported (refs. 53 and 54).

Dementia

Dementing disorders such as Alzheimer's disease, multi-infarct dementia, and Parkinson's disease are usually accompanied by prolongation of N2 and P3 (refs. 54 to 58).

Psychiatric disorders

Both N2 and P3 amplitudes have been consistently reported to be reduced in amplitude in schizophrenia (refs. 59 to 63) and depression (refs. 55 and 61). N2 and P3 latency are usually reported to be within normal limits in these disorders, although there have been reports of mild slowing in schizophrenic patients (refs. 55 and 63). Since N2 and P3 latency are usually within normal range in schizophrenia, while RT is slowed, this particular type of psychopathology may reflect disturbances of response selection and execution more than stimulus evaluation (ref. 64).

Correlation of N2-P3 with Neuropsychological Measures

Few EP studies provide behavioral or intellectual descriptions of patient groups beyond diagnosis. In the case of dementia, groups under study were often heterogeneous in diagnosis as well as severity. Specific intellectual or psychiatric disturbances relevant to such constructs as attention, learning, or degree of depression are seldom measured or correlated with specific EP changes. Consequently, the specific behavioral referents of variations in the N2-P3 complex due to brain dysfunction remain to be elucidated. Several recent studies of Parkinson's disease, a neurological disorder associated with varying degrees of motoric, intellectual, and psychiatric disturbance, have examined such patterns. The latency of P3 in Parkinson's disease is correlated with mental tests requiring cognitive effort and learning, and is less related to general measures of IQ, immediate memory span, depression or motor dysfunction (refs. 57 and 58). These results suggest that N2 and P3 changes associated with brain dysfunction may index specific types of cognitive and behavioral disturbance, in the same way that N2 and P3 characteristics in experimental paradigms vary with specific types of task demands.

Summary

The N2-P3 complex is delayed over the course of normal aging, and further delayed in dementing disorders associated with diffuse brain damage. In Parkinson's disease, P3 latency changes correlate with deficits in learning and tasks requiring cognitive effort. Psychiatric disorders, on the other hand, are consistently associated with reduction in N2-P3 amplitude, with relatively normal component latencies. This pattern of results may indicate that N2-P3 latency prolongation is a marker for clinically significant slowing of mental processes, or memory deficits, while diminished amplitude is associated with disorders affecting attention, motivation or arousal. The finding that seizure patients show increased P3 amplitude is consistent with the notion that P3 amplitude is a measure of CNS arousal (ref. 65).

Pharmacological Effects

The N2-P3 complex is differentially reactive to CNS stimulants and anticholinergic agents. Methylphenidate speeds RT without affecting P3 latency in young adults and children with attention disorders. This pattern suggests that methylphenidate speeds response generation, but does not affect stimulus evaluation processes (ref. 66). D-amphetamine, on the other hand, reduces both P3 latency and RT latency. These effects were not reduced by administering propranolol (ref. 67). The effect of d-amphetamine on P3 latency did not interact with stimulus complexity.

Scopolamine, an anti-cholinergic agent, slows both P3 and RT latency (ref. 66). At high levels, scopolamine abolishes P3 response and causes severe learning deficits, despite accurate task performance and retained immediate memory span (ref. 68).

These results again demonstrate the power the N2-P3, in conjunction with reaction time, to provide chronometric probes of the locus of variation in human performance. The effects of anti-cholinergic agents on the N2-P3

complex suggest that N2-P3 slowing may reflect breakdown in attentional and learning processes, similar to its significance in clinical disorders of the CNS.

The Cognitive Significance of the N2-P3 Complex

The P3 component has been described as indexing uncertainty (ref. 2), significance, information delivery (ref. 3), orienting (ref. 16) expectancy (ref. 15), equivocation (ref. 69), stimulus evaluation (refs. 23 and 29), context or schema updating (ref. 49), and value or meaning (ref. 1). This multiplicity of hypotheses regarding the functional significance of P3 reflects the diverse range of experimental manipulations which can affect P3 amplitude, latency, or both features. As is evident from the preceding review, the N2 component is reactive to many of the same factors as P3, although it may represent a more automatic phase of stimulus evaluation. Donchin (ref. 49) suggested that the P3 component may represent the CNS equivalent of a subroutine, which is invoked in a variety of cognitive operations. Alternatively, since the P3 may not consist of a single component, but rather the sum of a number of components overlapping in time (ref. 1), the characteristics of the P3 complex may index more than a single CNS function.

A model of P3 amplitude which assumes multiple determinants has been developed by Johnson (1986). Johnson (ref. 70) proposed that P3 amplitude is determined by three factors: subjective probability, stimulus meaning, and information transmission. Subjective probability is a joint function of global and sequential expectancies, as previously modeled by K. C. Squires and colleagues (ref. 15). Stimulus meaning is a function of task complexity, stimulus complexity, and stimulus value. Johnson proposed that subjective probability and stimulus meaning have an additive relationship, while both have a multiplicative relationship with information transmission. He makes the intriguing suggestion that subjective probability is an automatic process, while stimulus meaning is a controlled process.

The Assessment of Human Performance

The utility of the N2-P3 complex as a probe of CNS processes associated with stimulus evaluation, attentional variation, and mental load has been repeatedly demonstrated over the past two decades. Clinical and pharmacological evidence suggests that these measures are also sensitive to global changes in the information processing capacity of the CNS due to brain dysfunction. The effect of common stressors on human performance, such as fatigue, boredom, noise, or sleep deprivation on the N2-P3 complex has received much less attention. Further research is needed to elucidate how such stressors impact on the N2-P3 complex, and how this impact influences task performance. The inclusion of subjective measures of mood, arousal, and personality as setting variables in experiments may permit the development of multifactorial models of the determinants of psychophysiological response. Unlike machine information processing systems, human performance is modulated by biological and personality factors. Psychophysiological measures may provide markers for such influences.

In the evaluation of human performance, behavioral and subjective measures of performance are readily available. As Donchin (ref. 71) has argued, given the constraints and costs imposed by EP assessment of CNS function, EPs should be used only when they provide information which is not easily available from traditional indices of performance. The foregoing review of the N2-P3 complex suggests several applications in which unique information can be derived from EP measurement.

1. Evaluation of the time course of stimulus evaluation processes as distinct from response selection and execution.

2. Electrophysiological assessment of the attentional impact of infrequent events.

3. Measurement of workload specifically related to perceptual capacity. The auditory oddball task provides a relatively unobtrusive measure of secondary task processing. In addition, P3 amplitude may provide a direct measure of perceptual workload.

4. Characterizing the salience of events to an operator without requiring a behavioral response.

5. Identifying the time points in sensory and perceptual processing when pharmacological manipulations become effective.

6. Assessing the integrity of brain function.

Methodological Considerations

EP component identification and analysis

A variety of analytic techniques have been used to identify and measure components of the N2-P3 complex. The lack of consensus on identification and quantitative characterization of EP components, and the difficulty of discriminating variations in the latency of these components from single trials, has been a cause of continued concern and the application of diverse analytic techniques to EPs. (See Sutton and Ruchkin, 1984 (ref. 1), for an excellent discussion of the problems of component definition.) Popular analytic approaches include Woody filtering, subtraction waveforms, digital filtering, principal components analysis, peak-picking, and single-trial latency adjustment. Despite the obvious methodological concerns demonstrated by investigators, however, the experimental and clinical effects reviewed above are remarkably robust.

The most serious problem in reviewing and integrating studies in the literature is not, in the opinion of this reviewer, the difficulty in identifying the central phenomena of interest (although mapping the N2-P3 complex onto experimental factors and mental functions remains a vigorous and productive enterprise after two decades of activity). Rather, it is the tendency of experimenters to focus a priori on components of interest, and ignore other potentially informative components in the EP waveforms. Consequently, it is not unusual to read studies involving similar experimental manipulations which focus on P3 measures, and ignore earlier components, or conversely, measure early components, such as processing

negativities, without measuring later components. As a basic guideline, given the differential reactivity of EP components to stimulus properties and task demands, the major components of the N2-P3 complex (N2, P3, Slow Wave) should be measured, as well as at least one representative exogenous component (e.g. P100 with visual stimuli; N1 with auditory stimuli). Averaged EPs for each experimental conditions should be displayed before transformations such as principal components analysis are used. Indices of behavioral performance should be used in conjunction with EP responses when variations in task demands occur that may impact on response selection. A survey of papers presented at the Eighth International Conference on Event-Related Potentials of the Brain (ref. 72) suggests the field is moving toward greater specificity of measurement applied over the entire recorded EP epoch.

Ecologically Valid Experiments

The first phase of N2-P3 investigations, extending from perhaps 1965 to 1980, generally used stimuli with simple physical properties (e.g. tones, clicks, simple figures) and varied the stimuli on precise dimensions (e.g. intensity, probability, frequency). The benefit of this approach was a high degree of replicability across different laboratories, and the easy application of psychophysical, signal detection, and information processing paradigms. Moreover, since information processing was the dominant model of interpretation, semantic qualities of stimuli were not easily incorporated into analysis. Since the late 1970s, however, increasingly complex linguistic and visual stimulus paradigms have been utilized, presumably as consequence of investigators' confidence in their understanding of the basic characteristics of the N2-P3 complex. As the functional characteristics of these components have become understood, they have begun to be used as a tool for the understanding of mental processes, rather than being the explicit object of inquiry in an experiment. The evolution of EPs from an object of inquiry to a tool of inquiry has important implications for the investigation of human performance. Until this evolution occurred, application of EP measures to task analysis in engineering psychology would be a uninterpretable.

Developing more naturalistic tasks and environments will be an important step in using EPs to probe the CNS mechanisms modulating human performance. The constraints of EP analysis (the use of electrodes, electrical shielding, physiological amplifiers, analog or digital recording), the need for many trials to accrue an interpretable average, and the short time window of investigation limit the applicability of this technique. When the technique can be applied to a task, the stimuli, temporal frame, and environmental context should be as close as possible to the performance environment of interest.

Prediction of performance

The N2-P3 complex has usually been correlated with behavioral measures recorded concurrently in time. Prediction of subsequent human performance levels has seldom been a focus of investigation. It would be of great interest if properties of the N2-P3 complex might reflect an individual's general attentional or cognitive capabilities, and whether alterations in the N2-P3 complex in a serial task might reflect the probability of

subsequent lapses in attention. The sensitivity of the N2-P3 complex to brain dysfunction in clinical populations suggests it might show a similar sensitivity to diffuse changes in the CNS system in healthy individuals under unusual stress.

Summary

Two decades of productive research have demonstrated that the N2-P3 complex, and other endogenous components of the human EP (ref. 73), provide a set of tools for the investigation of human perceptual and cognitive processes. These multidimensional measures of CNS bioelectrical activity respond to a variety of environmental and internal factors which have been experimentally characterized. Their application to the analysis of human performance in naturalistic task environments is just beginning. Converging evidence suggests that the N2-P3 complex reflects processes of stimulus evaluation, perceptual resource allocation, and decision-making that proceed in parallel, rather than in series, with response generation.

Utilization of these EP components may provide insights into the CNS mechanisms modulating task performance unavailable from behavioral measures alone. The sensitivity of the N2-P3 complex to neuropathology, psychopathology, and pharmacological manipulation suggests that these components might provide sensitive markers for the effects of environmental stressors on the human CNS.

Acknowledgements

We would like to thank the following institutions for support: NIA Grant 1-P50-OAG05134, Alzheimer Disease Research Center; the Friedman Foundation; the University of Massachusetts Medical Center Scientific Council; and the Sterling Morton Charitable Trust.

References

1. Sutton, S., Ruchkin, D.S.: The Late Positive Complex: Advances and New Problems. In Karrer, R., Cohen, J., Tueting, P. (Eds.), *Brain and Information: Event-Related Potentials*. Annals of the New York Academy of Sciences, vol. 425, 1984, pp. 1-23.
2. Sutton, S., Braren, R., Zubin, J., John, E.R.: Evoked-Potential Correlates of Stimulus Uncertainty. *Science*, vol. 150, 1965, pp. 1187-1188.
3. Sutton, S., Tueting, P., Zubin, J., John, E.R.: Information Delivery and the Sensory Evoked Potential. *Science*, vol. 155, 1967, pp. 1436-1439.
4. Squires, N.K., Squires, K.C., Hillyard, S.A.: Two Varieties of Long-Latency Positive Waves Evoked by Unpredictable Auditory Stimuli in Man. *Electroencephalography and Clinical Neurophysiology*, vol. 38, 1975, pp. 387-401.
5. Simson, R., Vaughan, H.G., Ritter, W.: The Scalp Topography of Potentials Associated with Missing Visual or Auditory Stimuli. *Electroencephalography and Clinical Neurophysiology*, vol. 40, 1976, pp. 33-42.
6. Simson, R., Vaughan, H.G., Ritter, W.: The Scalp Topography of Potentials in Auditory and Visual Discrimination Tasks. *Electroencephalography and Clinical Neurophysiology*, vol. 42, 1977, pp. 528-535.
7. Naatanen, R., Simpson, M., Loveless, N.E.: Stimulus Deviance and Event-Related Brain Potentials. *Biological Psychology*, vol. 14, 1982, pp. 53-98.
8. Squires, N.K., Halgren, E., Wilson, C. and Crandall, P.: Human Endogenous Limbic Potentials: Cross-modality and Depth/Surface Comparisons in Epileptic Subjects. In Gaillard, A.W.K., Ritter, W. (Eds.), *Tutorials in Event Related Potential Research: Endogenous Components*. New York: North-Holland, 1983, pp. 217-232.
9. Okada, Y.C., Kaufman, L., Williamson, S.J.: The Hippocampal Formation as a Source of the Slow Endogenous Potentials. *Electroencephalography and Clinical Neurophysiology*, vol. 55, 1983, pp. 417-426.
10. Wood, C.C., McCarthy, G.: A Possible Frontal Lobe Contribution to Scalp P300. In Rohrbaugh, J.W., Johnson, R., Parasuraman, R. (Eds.), *Eighth International Conference on Event-Related Potentials of the Brain: Research Reports*. Stanford, 1986, pp. 164-166.
11. Duncan-Johnson, C., Donchin, E.: On Quantifying Surprise: The Variation of Event-Related Potentials with Subjective Probability. *Psychophysiology*, vol. 14, 1977, pp. 456-467.
12. Squires, N.K., Sanders, D., Wanser, R.: Comparison of Attend and Non-

Attend Paradigms for the Evaluation of ERP Changes in Normal Aging and Neurological Dysfunction. In Rohrbaugh, J.W., Johnson, R., Parasuraman, R. (Eds.), Eighth International Conference on Event-Related Potentials of the Brain: Research Reports. Stanford, 1986, pp. 137-139.

13. Campbell, K.B., Courchesne, E., Picton, T.W., Squires, K.C.: Evoked Potential Correlates of Human Information Processing. *Biological Psychology*, vol. 8, 1979, pp. 45-68.
14. Friedman, D. B., Hakarem, G., Sutton, S., Fleiss, J. L.: Effect of Stimulus Uncertainty on the Pupillary Dilatation Response and the Vertex Evoked Potential. *Electroencephalography and Clinical Neurophysiology*, vol. 34, 1973, pp. 475-484.
15. Squires, K.C., Wickens, C., Squires, N.K., Donchin, E.: The Effect of Stimulus Sequence on the Waveform of the Cortical Event-Related Potential. *Science*, vol. 193, 1976, pp. 1142-1146.
16. Ritter, W., Vaughan, H.G., Costa, L.D.: Orienting and Habituation to Auditory Stimuli: A Study of Short Term Changes in Averaged Evoked Responses. *Electroencephalography and Clinical Neurophysiology*, vol. 25, 1968, pp. 550-556.
17. Rohrbaugh, J.W. The Orienting Reflex: Performance and CNS Manifestations. In R. Parasuraman (Ed.), *Varieties of Attention*. New York: Academic Press, 1984.
18. Pritchard, W.S., Brandt, M.E., Shappell, S.A., O'Dell, T., Barratt, E.S.: No Decrement in Visual P300 Amplitude During Extended Performance of the Oddball Task. *International Journal of Neuroscience*, vol. 29, 1986, pp. 199-204.
19. Courchesne, E., Courchesne, R.Y., Hillyard, S.A.: The Effect of Stimulus Deviation on P3 Waves to Easily Recognized Stimuli. *Neuropsychologia*, vol. 16, 1978, pp. 189-199.
20. Donchin, E., Heftley, E., Hillyard, S.A., Loveless, N., Maltzman, I., Ohman, A., Fosler, F., Ruchkin, D., Siddle, D.: Cognition and Event-Related Potentials: II. The Orienting Reflex and P300. In Karrer, R., Cohen, J., Tueting, P. (Eds.), *Brain and Information: Event Related Potentials*. *Annals of the New York Academy of Sciences*, vol. 425, 1984, pp. 39-57.
21. Rosler, F.: Central and Peripheral Correlates of Orienting and Habituation. In Rohrbaugh, J.W., Johnson, R., Parasuraman, R. (Eds.), Eighth International Conference on Event-Related Potentials of the Brain: Research Reports. Stanford, 1986, pp. 254-256.
22. Loveless, N.: Event-Related Slow Potentials of the Brain as Expressions of the Orienting Function. In H. D. Kimmel, E. H. van Olst, J. F. Orlebeke, (Eds.), *The Orienting Reflex in Humans*. New York: Erlbaum, 1979.
23. Kutas, M., McCarthy, G., Donchin, E.: Augmenting Mental Chronometry:

- The P300 as a Measure of Stimulus Evaluation Time. *Science*, vol. 197, 1977, pp. 792-795.
24. Ritter, W., Vaughan, H.G., Friedman, D.: A Brain Event Related to the Making of a Sensory Discrimination. *Science*, vol. 203, 1979, pp. 1358-1361.
 25. Goodin, D.S., Aminoff, M.J.: The Relationship Between the Evoked Potential and Brain Events in Sensory Discrimination and Motor Response. *Brain*, vol. 107, 1984, pp. 241-251.
 26. Goodin, D.S., Aminoff, M.J., Mantle, M.M.: Subclasses of Event-Related Potentials: Response-Locked and Stimulus-Locked Components. *Annals of Neurology*, vol. 20, 1986, pp. 603-609.
 27. Papanicolaou, A.C., Loring, D.W., Raz, N., Eisenberg, H.M.: Relationship Between Stimulus Intensity and the P300. *Psychophysiology*, vol. 22, 1985, pp. 326-329.
 28. Ritter, W., Simson, R., Vaughan, H.G.: Association Cortex Potentials and Reaction Time in Auditory Discrimination. *Electroencephalography and Clinical Neurophysiology*, vol. 33, 1972, pp. 547-555.
 29. Squires, N.K., Donchin, E., Squires, K.C.: Bisensory Stimulation: Inferring Decision-Related Processes from the P300 Component. *Journal of Experimental Psychology: Human Perception and Performance*, vol. 3, 1977, pp. 299-315.
 30. Goodin, D.S., Squires, K.C., Starr, A.: Variations in Early and Late Event-Related Components of the Auditory Evoked Potential with Task Difficulty. *Electroencephalography and Clinical Neurophysiology*, vol. 55, 1983, pp. 680-686.
 31. Walton, P., Halliday, R., Naylor, H., Callaway, E.: Stimulus Intensity, Contrast and Complexity Have Additive Effects on P3 Latency. In Rohrbaugh, J.W., Johnson, R., Parasuraman, R. (Eds.), *Eighth International Conference on Event-Related Potentials of the Brain: Research Reports*. Stanford, 1986, pp. 409-411.
 32. McCarthy, G., Donchin, E.: A Metric for Thought: A Comparison of P300 Latency and Reaction Time. *Science*, vol. 211, 1981, pp. 77-80.
 33. Squires, K.C., Hillyard, S.A., Lindsay, P.A.: Vertex Potentials Evoked During Auditory Signal Detection: Relation to Decision Criteria. *Perception & Psychophysics*, vol. 14, 1973, pp. 265-272.
 34. Squires, K.C., Squires, N.K.: Vertex Evoked Potentials in a Rating-Scale Detection Task: Relation to Signal Probability. *Behavioral Biology*, vol. 13, 1975, pp. 21-34.
 35. Squires, K.C., Squires, N.K., Hillyard, S.A.: Decision-Related Cortical Potentials During an Auditory Signal Detection Task with Cued Observation Intervals. *Journal of Experimental Psychology: Human Perception and Performance*, vol. 1, 1975, pp. 268-279.

36. Parasuraman, R., Beatty, J.: Brain Events Underlying Detection and Recognition of Weak Sensory Signals. *Science*, vol. 210, 1980, pp. 80-83.
37. Posner, M.I.: Psychobiology of Attention. In Gazzaniga, M.S., Blakemore, C. (Eds.), *Handbook of Psychobiology*. New York: Academic Press, 1975.
38. Wickens, C., Kramer, A., Vanasse, L., Donchin, E.: Performance of Concurrent Tasks: A Psychophysiological Analysis of the Reciprocity of Information-Processing Resources. *Science*, vol. 226, 1983, pp. 1080-1082.
39. Warren, L.R., Marsh, G.R.: Changes in Event Related Potentials During Processing of Stroop Stimuli. *International Journal of Neurosciences*, vol. 9, 1979, pp. 217-223.
40. Israel, J.B., Chesney, G.L., Wickens, C.D., Donchin, E.: P300 and Tracking Difficulty: Evidence for Multiple Resources in Dual-Task Performance. *Psychophysiology*, vol. 17, 1980, pp. 259-273.
41. Israel, J.B., Wickens, C.D., Chesney, G.L., Donchin, E.: The Event-Related Brain Potential as an Index of Display-Monitoring Workload. *Human Factors*, vol. 22, 1980, pp. 211-224.
42. Horst, R.L., Munson, R.C., Ruchkin, D.S.: ERP Processing Negativities Related to Workload. In Rohrbaugh, J.W., Johnson, R., Parasuraman, R. (Eds.), *Eighth International Conference on Event-Related Potentials of the Brain: Research Reports*. Stanford, 1986, pp. 350-352.
43. Schneider, W., Schiffrin, R. M.: Controlled and Automatic Human Information Processing: I. Detection, Search and Attention. *Psychological Review*, vol. 84, 1977, pp. 1-66.
44. Hoffman, J.E., Simons, R.F., Houck, M.R.: Event-Related Potentials During Controlled and Automatic Target Detection. *Psychophysiology*, vol. 20, 1983, pp. 625-632.
45. Kramer, A., Schneider, W., Fisk, A., Donchin, E.: The Effects of Practice and Task Structure on the Components of the Event-Related Brain Potential. *Psychophysiology*, vol. 23, 1986, pp. 33-47.
46. Neville, H.J., Snyder, E., Woods, D.L., Galambos, R.: Recognition and Surprise Alter the Human Visual Evoked Response. *Proceedings of the National Academy of Sciences USA*, vol. 79, 1982, pp. 2121-2123.
47. Sanquist, T.F., Rohrbaugh, J.W., Syndulko K., Lindsley, D.B.: Electro cortical Signs of Levels of Processing: Perceptual Analysis and Recognition Memory. *Psychophysiology*, vol. 17, 1980, pp. 568-576.
48. Johnson, R., Pfefferbaum, A., Kopell, S.: P300 and Long-Term Memory: Latency Predicts Recognition Performance. *Psychophysiology*, vol. 22, 1985, pp. 497-507.

49. Donchin, E.: Surprise!...Surprise ? *Psychophysiology*, vol. 8, 1981, pp. 493-513.
50. Fabiani, M., Karis, D., Donchin, E.: P300 and Recall in an Incidental Memory Paradigm. *Psychophysiology*, vol. 23, 1986, pp. 298-308.
51. Karis, D., Fabiani, M., Donchin, E.: P300 and Memory: Individual Differences in the Von Restorff Effect. *Cognitive Psychology*, vol. 16, 1984, pp. 177-216.
52. Friedman, D., Sutton, S.: Event-Related Potentials During Continuous Recognition Memory. In Rohrbaugh, J.W., Johnson, R., Parasuraman, R. (Eds.), *Eighth International Conference on Event-Related Potentials of the Brain: Research Reports*. Stanford, 1986, pp. 227-229.
53. Goodin, D.S., Squires, K.C., Henderson, B.H., Starr, A.: Age-Related Variations in Evoked Potentials to Auditory Stimuli in Normal Subjects. *Electroencephalography and Clinical Neurophysiology*, vol. 44, 1978, pp. 447-458.
54. Syndulko, K., Hansch, E.C., Cohen, S.N., Pearce, J.W., Goldberg, Z., Montan, B., Tourtellotte, W.W. and Potvin, A.R.: Long-Latency Event-Related Potentials in Normal Aging and Dementia. In Courjon, J., Mauguire, F. and Revol, M. (Eds.), *Clinical Applications of Evoked Potentials in Neurology*. Raven Press: New York, 1982, pp. 278-285.
55. Pfefferbaum, A., Wenegrat, B.G., Ford, J.M., Roth, W.T., Kopell, B.S.: Clinical Application of the P3 Component of the Event-Related Potentials. II. Dementia, Depression and Schizophrenia. *Electroencephalography and Clinical Neurophysiology*, vol. 59, 1984, pp. 104-124.
56. Goodin, D.S., Squires, K.C., Starr, A.: Long Latency Event-Related Components of the Auditory Evoked Potential in Dementia. *Brain*, vol. 101, 1978, pp. 635-648.
57. Hansch, E.C., Syndulko, K., Cohen, S.N., Goldberg, Z.I., Potvin, A.R. and Tourtellotte, W.W.: Cognition in Parkinson Disease: An Event-Related Potential Perspective. *Annals of Neurology*, vol. 11, 1982, pp. 599-607.
58. O'Donnell, B.F., Squires, N.K., Martz, M.J., Chen, J.R., Phay, A.J.: Evoked Potential Abnormalities and Neuropsychological Performance in Parkinson's disease. *Biological Psychology*, vol. 24, 1987, pp. 23-37.
59. Roth, W.T., Horvath, T.B., Pfefferbaum, A., Kopell, B.S.: Event-Related Potentials in Schizophrenics. *Electroencephalography and Clinical Neurophysiology*, vol. 48, 1980, pp. 127-139.
60. Verleger, R., Cohen, R.: Effects of Certainty, Modality Shift and Guess Outcome on Evoked Potentials and Reaction Times in Chronic Schizophrenics. *Psychological Medicine*, vol. 8, 1978, pp. 81-93.

61. Levit, R.A., Sutton, S. and Zubin, J.: Evoked Potential Correlates of Information Processing in Psychiatric Patients. *Psychological Medicine*, vol. 3, 1973, pp. 487-494.
62. Pass, H.L., Klorman, R., Salzman, L.F., Klein, R.H., Kasberg, G.B.: The Late Positive Component of the Evoked Response in Acute Schizophrenics During a Test of Sustained Attention. *Biological Psychiatry*, vol. 15, 1980, pp. 9-20.
63. Brecher, M., Porjesz, B., Begleiter, H.: The N2 Component of the Event-Related Potential in Schizophrenic Patients. *Electroencephalography and Clinical Neurophysiology*, vol. 66, 1987, pp. 369-375.
64. Duncan-Johnson, C.C., Roth, W., Koppell, B.S.: Effects of Stimulus Sequence on P300 and Reaction Time in Schizophrenics. In Karrer, R., Cohen, J., Tueting, P. (Eds.), *Brain and Information: Event-Related Potentials*. *Annals of the New York Academy of Sciences*, vol. 425, 1984, pp. 570-577.
65. Drake, M.E., Burgess, R.J., Gelety, T.J., Ford, C.E., Brown, M.E.: Long-Latency Auditory Event-Related Potentials in Epilepsy. *Clinical Electroencephalography*, vol. 17, 1986, pp. 10-13.
66. Callaway, E.: Human Information Processing: Some Effects of Methylphenidate, Age, and Scopolamine. *Biological Psychology*, vol. 19, 1984, pp. 649-662.
67. Halliday, R., Naylor, H., Callaway, E., Yano, L., Walton, D.: D-Amphetamine Speeds Both Stimulus and Response Processing. In Rohrbaugh, J.W., Johnson, R., Parasuraman, R. (Eds.), *Eighth International Conference on Event-Related Potentials of the Brain: Research Reports*. Stanford, 1986, pp. 93-95.
68. Hammond, E.J., Meador, K.J., Aung-Din, R., Wilder, B.J.: Cholinergic Modulation of Human Event-Related Potentials. *Neurology*, vol. 37, 1987, pp. 346-350.
69. Ruchkin, D.S., Sutton, S.: Equivocation and P300 Amplitude. In Otto, D. (Ed.), *Multidisciplinary Perspectives in Event-Related Brain Potential Research*. EPA-600/9-77-043. U.S.G.P.O.: Washington, D.C., 1978, pp. 175-177.
70. Johnson, R.: A Triadric Model of P300 Amplitude. *Psychophysiology*, vol. 23, 1986, pp. 367-384.
71. Donchin, E., Kramer, A., Wickens, C.: Applications of Brain Event-Related Potentials to Problems in Engineering Psychology. In Coles, M.G.H., Donchin, E., Porges, S.W. (Eds.), *Psychophysiology: Systems, Processes, and Applications*. New York: Guilford, 1986, pp. 702-718.
72. Rohrbaugh, J.W., Johnson, R., Parasuraman, R. (Eds.), *Eighth International Conference on Event-Related Potentials of the Brain: Research Reports*. Stanford, 1986.

73. Hillyard, S.A., Kutas, M.: Electrophysiology of Cognitive Processing. Annual Review of Psychology, vol. 34, 1983, pp. 33-61

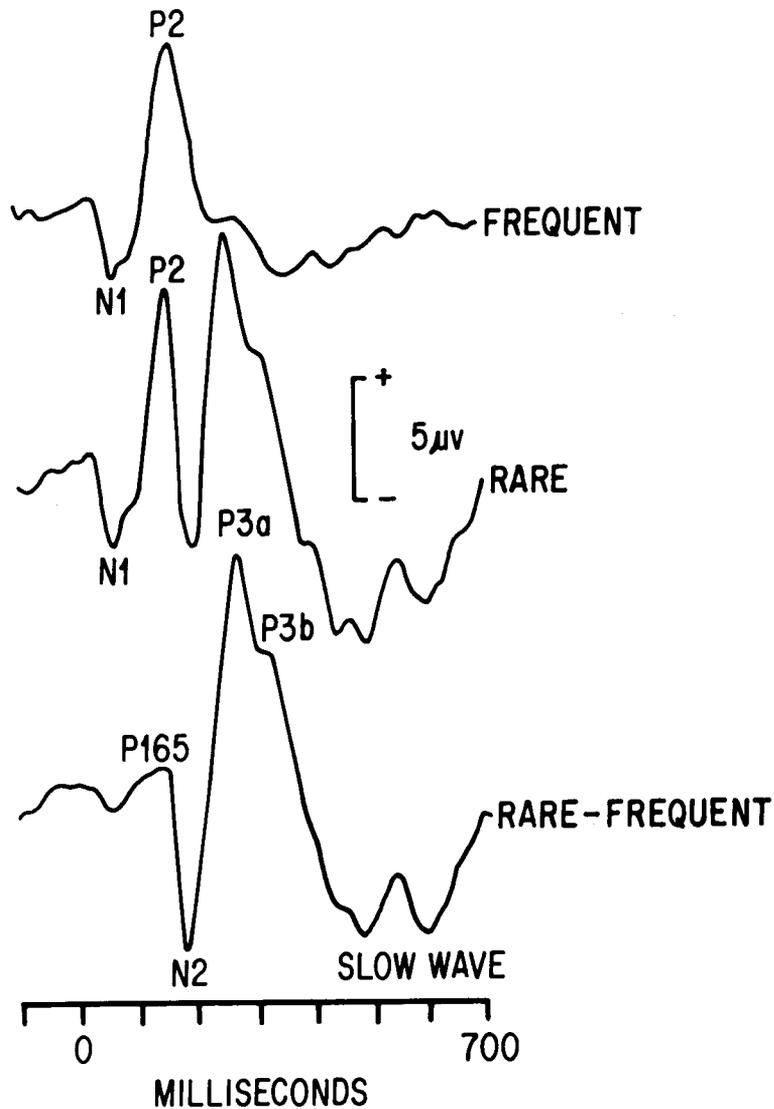


Figure 1. Evoked potentials averaged from frequent 1000 Hz tones and rare target 2000 Hz tones (probability = .10). Frequent tones elicit the N1-P2 components, while rare tones elicit both the N1-P2 and endogenous N2-P3 components. Subtraction of waveforms generated by rare tones from frequent tone waveforms isolates the endogenous components (P165, N2, P3a, P3b, and Slow Wave).