

THE USE OF EVENT-RELATED POTENTIALS IN THE STUDY OF BRAIN ASYMMETRIES

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(Received June 18, 1987)

The utility of event-related brain potentials (ERPs) in the study of hemispheric specialization is discussed in the context of three experimental cases: the application of motor potentials to the "continuous flow" model of human information processing, investigations of the role of early experience in cerebral organization, and hemispheric asymmetries in phonemic recoding during reading. The importance of the electrical reference in ERP records is stressed.

Keywords: event-related potential, hemispheric asymmetry, reference electrode, motor potential

It has been known for quite a long time that the two hemispheres of the human cortex are not functionally equivalent. Nonetheless, it has proved extremely difficult to specify the ways in which the hemispheres are similar and the ways in which they are different. This paper addresses a few of the methodological and conceptual limits of the event-related potential (ERP) technique and describes the potential benefits and pitfalls of this approach by reference to a few specific experiments. In so doing, we hope to show both the potential contributions of the ERP to our understanding of cerebral specialization and the nature of the information that has already been provided by this methodology.

The ERP is a partial record of brain physiology; a left-right ERP asymmetry on the scalp can be taken as an indication of an underlying asymmetry in brain activity, provided all spurious sources for the asymmetry have been ruled out. When this physiological activity can be related to a psychological concept or variable, it will also be possible to interpret the cognitive significance of its asymmetry. The design of an experiment which utilizes an asymmetric ERP component can thus begin with an emphasis on either its physiologic or cognitive basis. On the one hand, an ERP investigator may choose to measure a component which reflects a given fact about anatomical-physiological asymmetries of brain organization and study the sensitivity of this component to various psychological manipulations. On the other hand, an experimenter may start with a component which has been empirically correlated with a psychological process and infer underlying physiological asymmetries based on the component's distribution across the scalp.

An excellent example of the first approach is the work of Michael Coles and colleagues at the University of Illinois. Coles et al. (1985) have used the latency of a physiologic response, the readiness potential, which has been related to the psychological concept of motor preparation to make inferences about the flow of information in a reaction time (RT) task. The goals of these experimenters have

Based on a presentation at the Twenty-Sixth Annual Meeting of the Society for Psychophysiological Research, Montreal, Quebec, 1986 (Kutas & Neville, 1986). Some of the work reported here was supported by grants from NSF (BNS83-09243) and NICHD (HD 22614). C. Van Petten is supported by an NSF Graduate Fellowship. M. Kutas is supported by a Research Career Development Award from NIH (MH 00322).

been to: (1) investigate the time course of motor preparation, (2) assess the role of expectancy on preparation, and (3) determine the nature of the processes that lead to response errors. This work has been used to contrast serial models of human information processing in which stimulus evaluation, decisions, motor preparation, and overt motor activity occur in discrete stages with a "continuous flow" model in which these stages of cognitive activity overlap in time (see Coles, Gratton, Bashore, Eriksen & Donchin, 1985; Gratton & Coles, 1986). ERPs have been particularly useful in dissociating these processes as the latency of the P300 component has been correlated with the duration of stimulus evaluation while the readiness potential has been related to motor preparation (Desmedt, 1977; Kornhuber & Deecke, 1980; Kutas, McCarthy & Donchin, 1977; McCarthy & Donchin, 1981).

The experimental paradigms of Coles et al. require the subject to respond with one hand for stimuli of one type, and the other hand for stimuli of a different type. This design capitalizes on the fact that the readiness potential on the scalp reflects the contralateral motor organization of the underlying cortex and is therefore typically observed to be largest at scalp sites opposite to the responding hand (Kutas & Donchin, 1977). Thus, the lateralization of this ERP component can be used to determine the balance and time course of motor preparation between the two hands as the subject acquires information from a visual display and prepares one or the other hand to make a response.

The work of Helen Neville and associates at the Salk Institute illustrates the experimental logic of the second approach whereby asymmetric ERPs can be utilized. Research in several laboratories has indicated that both psycholinguistic and attentional paradigms elicit asymmetric ERP components in normal subjects. Neville's goal has been to sharpen the functional definitions of these asymmetric components, clarify the cerebral specializations which underly them, and in particular, to investigate the influence of early experience on these functional and physiological asymmetries. Her recent experiments have involved comparisons of normally hearing and congenitally deaf individuals (Neville, Kutas, & Schmidt, 1982b; Neville, Schmidt, & Kutas, 1983; Neville & Lawson, 1987a, b, c). The results of these studies are too complex to be detailed here. Suffice it to say that asymmetric visual evoked potentials are elicited during the reading of isolated English words and English sentences, during the comprehension of American Sign Language (ASL), and during the detection of motion in the visual periphery. Some of these asymmetries are the same for deaf and hearing individuals, but others are not.

Neville has maintained that the differential ERP lateralities seen for congenitally deaf and normally hearing persons suggest that the two groups differ in some dimensions of functional brain organization. In itself, this is interesting but not very informative. A more important issue is to determine which aspect of congenital deafness accounts for these differences. Neville has considered: (1) the influence of auditory deprivation, (2) the acquisition of a visuospatial language (ASL) early in life rather than a phonetic one, (3) the fact that English is typically a second language for these subjects and that ERP responses to English stimuli may be altered due to an unsophisticated grasp of its syntax. Two approaches have been taken to dissociate these possibilities. One has been to collect behavioural and ERP data from hearing subjects who were raised in deaf families; these individuals have had normal auditory experience but learned ASL as a first language. A second approach has been to compare the ERPs of deaf subjects reading words and sentences in English versus ASL. These experimental manipulations have shown

that each of the aforementioned factors seem to make separate contributions to the differences between deaf and hearing ERPs.

The elegant experimental logic applied by Neville to relate ERP asymmetries to the role of early experience in brain organization illustrates a general point in this type of research: it is only possible to relate lateralized potentials to brain functions when there is a testable hypothesis as to what the functions are. In general, the availability of an answer is determined by the nature and specificity of the question.

Despite the successes of Cole and Neville, there are methodological hazards in the interpretation of asymmetric scalp potentials. We would like to discuss one of these, namely the possibility that the site chosen for the reference electrode is both active and asymmetric. Although well known, this possibility seems to be inadequately addressed more often than not. The most common electrical reference found in the ERP literature is linked mastoids/ears. Investigators do themselves a disservice in the use of this reference, especially if their primary interest is in hemispheric specialization. The theoretical reasons for this have been detailed by Katznelson (1981). Briefly, linking the mastoids does not result in an averaged mastoid lead, rather, it electrically shorts the two leads and forces them to be equipotential. Whenever the potentials at the two linked leads are not equivalent prior to linking, forcing them to be equipotential alters the voltage field. This disturbance of the field potentials around the head has consequences not only for the reference electrodes but also the potentials recorded at the "active" leads across the scalp. This problem is partially alleviated by putting a 10–20 kOhm resistor in series with each mastoid lead prior to linking. If the activity at the two mastoids is isopotential, then linking the leads is equivalent to using only one or the other as a reference. A recommendation: before using a mastoid reference, record from the left and right to decide if they are the same or different. The answer to this question, and the reference site that one ultimately chooses may determine the results of the experiment. This point can be illustrated by an experiment from our laboratory (Van Petten & Kutas, unpublished observations).

We were interested in the question of phonemic recoding during reading. A number of studies have suggested that readers are sensitive to the sound pattern of written words (Hillinger, 1980; Schulman, Hornak & Sanders, 1978), and we wanted to determine if this awareness of a word's phonology occurred prior to, subsequent to, or simultaneously with the awareness of a word's meaning. We expected that any ERP reflection of phonemic recoding might be asymmetric, as studies with commissurotomy patients have suggested that only the left hemisphere is capable of grapheme-to-phoneme conversion (Levy & Trevarthen, 1977; Zaidel, 1978).

A useful experimental tool to investigate the interaction of phonology and semantics are homophonic words, i.e., pairs of words which are pronounced the same, but have different spellings and meanings. In the present experiment, three types of word pairs were prepared (100 of each): related (e.g., "day-night") unrelated (e.g., "cat-table"), and "homophone unrelated" in which one member of a related pair was substituted for its homophonic relative (e.g., "reign-snow"). These stimuli were selected to capitalize on the sensitivity of the N400 component of the ERP to semantic relationships. We expected the unrelated pairs to elicit a larger N400 than related pairs as this effect has been shown in previous work with sequentially presented words (Bentin, McCarthy & Wood, 1985; Harbin, Marsh & Harvey, 1984; Kutas, 1985; Rugg, 1985). The condition of interest was the "homophone unrelated" as the amplitude and latency of an N400 in this condition might reveal the point at which the subjects realized that while the visual words

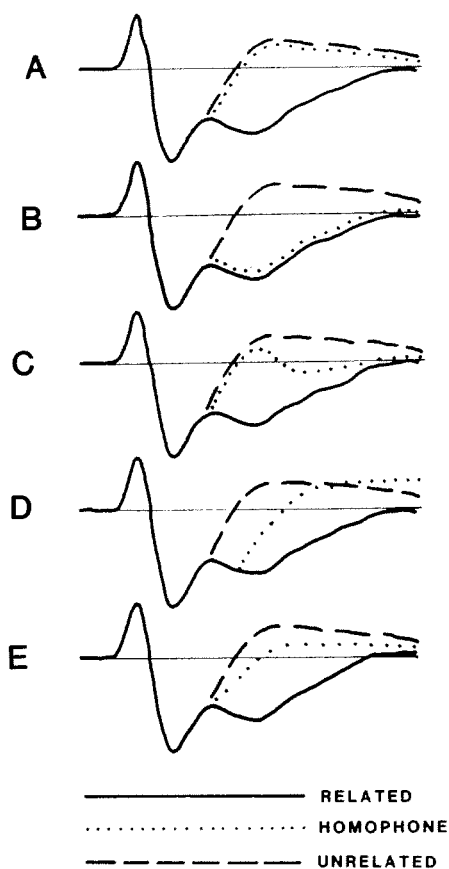


FIGURE 1 Schematic ERPs to illustrate some possible outcomes of the homophone experiment described in the text. In each case, unrelated word pairs elicit a larger N400 than related word pairs. In (A) the ERPs in the "homophone unrelated" and unrelated conditions elicit identical N400s, suggesting that the task did not elicit phonemic recoding of written words, or that the ERP was not sensitive to this operation. In (B) the "homophone unrelated" and related conditions are identical, suggesting that phonemic recoding occurs prior to the comprehension of meaning, and that only the phonemic representation is used to address the semantic lexicon. In (C) the "homophone unrelated" initially resembles the unrelated condition but later in the recording epoch begins to resemble the related condition, suggesting that phonemic recoding occurs subsequent to the initial comprehension of meaning but is still used to address the semantic lexicon. In (D) the "homophone unrelated" condition initially resembles the related condition, but elicits a long-latency N400 and so begins to resemble the unrelated condition. This outcome, like (B) would suggest that phonemic recoding occurs prior to the comprehension of meaning, but that the original visual-orthographic representation of a word is preserved and used to address the semantic lexicon sometime later. In (E) the "homophone unrelated" condition yields an N400 of identical onset latency but reduced amplitude, relative to the unrelated condition. This would suggest that phonemic recoding occurs prior to the comprehension of meaning, but that the phonemic and orthographic representations of a word can be used to address the semantic lexicon in parallel.

were semantically unrelated, their phonemic representations were of two related words. Figure 1 illustrates the possible outcomes of this condition, and the conclusions that might be drawn.

Each word pair was presented visually so that one word fell to the right of a central point and the other to the left. Subjects were asked to indicate whether or not the words were semantically related with a delayed behavioural response. Trials which elicited an incorrect verbal response were not averaged, nor were those with excessive eye movements as determined by electrooculogram potentials recorded by electrodes around the eyes. The EEG was recorded with a bandpass of 0.01 to 35 Hz (half amplitude cutoff) with a sampling rate of 250 Hz.

Electrodes were placed at a midline parietal site (Pz), five pairs of lateral sites (F3, F4, C3, C4, P3, P4, T5, T6, O1 and O2) and the right mastoid, all referenced to the left mastoid. For 6 of the 24 subjects, a balanced noncephalic montage (sternum to seventh cervical vertebra) was also used as a recording site (Stephenson & Gibbs, 1951). Having electrodes at three possible reference sites, the left mastoid, the right mastoid, and the noncephalic montage allowed us to rereference the scalp channels to any one of the three off-line. This proved to be important; the results varied as a function of the reference site.

Figure 2 shows the grand average ERPs to the three types of word pairs recorded from a pair of lateral sites with three different mastoid references. Across all electrodes and references, there was a large difference between related and unrelated pairs; the unrelated pairs elicited a larger N400. The experimental question, however, concerned the similarity or dissimilarity of ERPs in the "homophone unrelated" condition to those in the unrelated condition. With a right

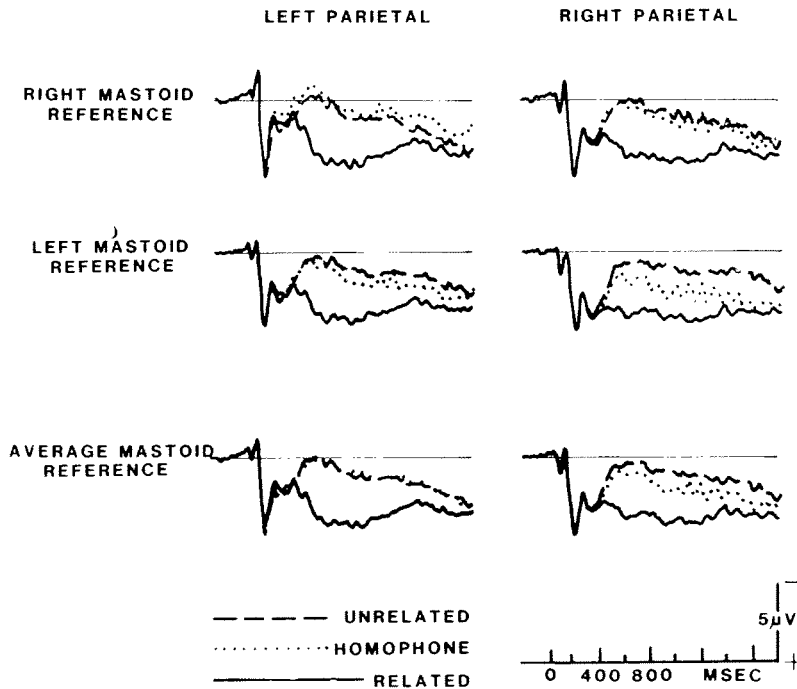


FIGURE 2 Grand average ERPs from 24 subjects recorded at P3 and P4. A comparison of the three columns shows the effects of re-referencing the same data to different electrode sites.

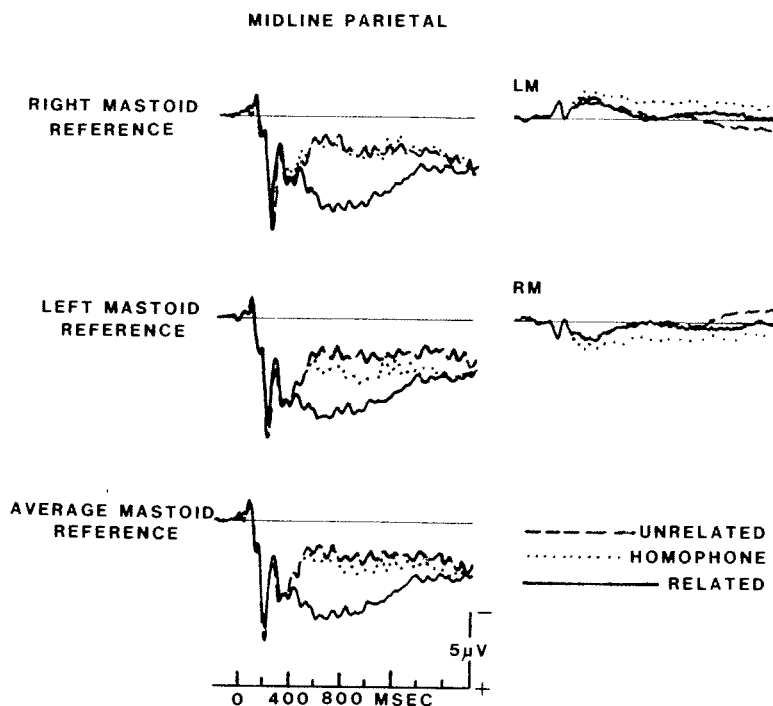


FIGURE 3 Grand average ERPs from 24 subjects recorded at Pz, right mastoid (RM) and left mastoid (LM). As in Figure 2, a comparison of the three columns shows the effects of rereferencing the same data to three different electrode sites.

mastoid reference, one would conclude that there was little or no difference; subjects are not influenced by the sound pattern of the homophones. With a left mastoid reference, one could reach very different conclusions; namely, that (1) the subjects did access the sound patterns of visual words as the ERPs to "homophone unrelated" pairs were more positive than those to unrelated pairs, (2) the grapheme-to-phoneme conversion process is at least somewhat lateralized since the ERP difference between "homophone unrelated" and unrelated was larger over the right hemisphere than the left and that (3) the activation of the words' sound patterns lagged behind access to their meaning as the additional positivity for the "homophone unrelated" pairs appears to begin somewhat later than the onset of the basic N400 effect for unrelated pairs. Finally, the use of a reference montage which was the average of left and right mastoids leads to conclusions which are somewhat similar to those with the right mastoid reference. However, the experimental effect with average-mastoid reference was considerably smaller, and apparent only over the right side of the head.

It is important to note that none of the foregoing conclusions are specific to the lateral distribution of the experimental effect. The midline electrode site was affected by the choice of reference in exactly the same way as the lateral sites (see Figure 3). Again, using a right mastoid reference results in no difference between the ERPs elicited by "homophone unrelated" and unrelated pairs, whereas using a left mastoid reference yields a substantial experimental effect, and the average mastoid reference yields a similar but substantially smaller experimental effect.

These ambiguous experimental results led us to one definite conclusion: the two mastoids were differentially active in this task. We had no way of knowing if one of the mastoids was relatively neutral with respect to the different experimental conditions, or if both electrodes were reflecting brain activity related to phonemic recoding. Additional subjects were run with a noncephalic recording montage in an attempt to resolve this question. While there was no guarantee that the noncephalic locations would be experimentally neutral, these electrodes were at least placed on the midline where we hoped they would be less sensitive to lateralized cerebral



FIGURE 4 Grand average ERPs from 6 subjects recorded at Pz, right mastoid (RM), and left mastoid (LM). As in Figures 2 and 3, a comparison of the three columns shows the effects of rereferencing the same data to different electrode sites.

activity. The ERPs from these six subjects are shown in Figure 4. It can be seen that the midline ERP referenced to a noncephalic montage is more similar to the left mastoid reference than to the right. While not definitive, we take this as an indication that the left mastoid was relatively less active than the right, and would be the better reference for this particular experiment.

The take-home message based on our experience remains the same: before choosing the reference for an experiment, record from several possible sites to determine the distribution of the experimental effects across the various recording

sites. It may be necessary to follow this procedure for any new experimental paradigm since it is rarely possible to predict in advance what relationship a possible reference site will have to a given ERP component. In the homophone experiment we noted that while the main experimental effect was dependent on the choice of reference, the occipital N1 was always larger on the left, regardless of reference (see Figure 5).

In summary, the ERP and its asymmetries can be used to answer questions about the functions of the two cerebral hemispheres. Our first experimental example, the work of Coles and colleagues shows how a reliable ERP asymmetry which reflects a known fact of physiology, namely contralateral motor control, can be used in a creative way to address a more general question about human information processing. Our second example, the work of Neville and colleagues, illustrates the use of ERPs in elucidating the significance and origins of asymmetric activity. Our final experimental case was meant to serve as a cautionary note to consider the role of the reference electrode in interpreting asymmetric brain potentials.

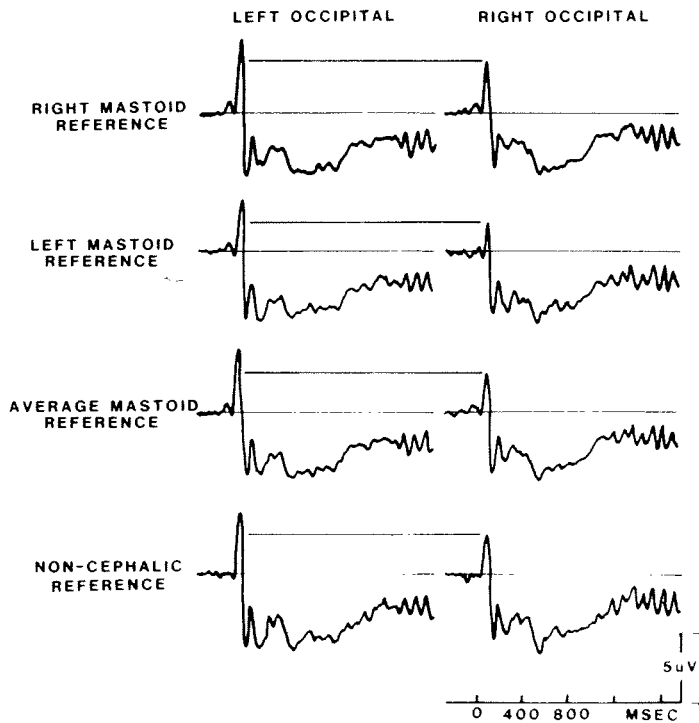


FIGURE 5 Grand average ERPs from the same data set as Figures 2 and 3, collapsed across experimental conditions. Sites O1 (left occipital) and O2 (right occipital) are shown to illustrate that the amplitude asymmetry of the first negative peak (at 140 ms poststimulus onset) is unaffected by the choice of reference electrode.

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