eration and competition may prove valuable for evaluating kinship theory (*25*) and for investigating mechanisms of kin recognition (*26*).

JAMES HANKEN*
Department of Zoology and Museum of Vertebrate Zoology, University of California, Berkeley 94720
PAUL W. SHERMAN
Section of Neurobiology and Behavior, Cornell University, Ithaca, New York 14850

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21. Of 30 proteins surveyed in liver, kidney, muscle, and blood, the following were monomorphic (the number of loci assayed is given in parentheses): lactate dehydrogenase (2), peptidase (3), glyceraldehyde phosphate dehydrogenase (1), phosphogluconate dehydrogenase (2), superoxide dismutase (1), diaphorase (1), malate dehydrogenase (2), carbonic anhydrase (1), malic enzyme (1), isocitrate dehydrogenase (2), α-glycerol-3-phosphate dehydrogenase (1), phosphoglucomutase (2), glutamate oxaloacetate transaminase (1), and glucose-6-phosphate dehydrogenase (1). The following loci were polymorphic (the number of alleles is given in parentheses): adenylate kinase (2), sorbitol dehydrogenase (3), mannose phosphate isomerase (2), adenosine deaminase (3), phosphoglucomutase 2 (2), glutamate oxaloacetate transaminase 1 (2), malic enzyme 1 (2), protein 1 (3), and protein 3 (2). There was no evidence of "null" alleles (alleles not detectable by electrophoresis) at any locus. Frequency of polymorphic loci was 33 percent and heterozygosity averaged 10.7 percent. For the six polymorphic loci that were resolvable in blood (Table 1), frequencies of homozygotes and heterozygotes agree with the Hardy-Weinberg expectation, computed from observed allele frequencies ($P \geq .9$ in all cases, χ^2 test).
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24. For the 1977 and 1978 data combined, at the adenosine deaminase locus the two-male and "infinite male" models predicted detection of 2.0 and 6.2 litters containing three paternal alleles, respectively; two litters were observed. At the protein 1 locus, detection of 4.9 and 10.6 litters was expected; seven litters were observed.
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* Present address: Department of Biology, Dalhousie University, Halifax, Nova Scotia, Canada B3H 4J1.

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Language-Related Potentials Specific to Human Language Cortex

Abstract. *Event-related potentials following silently named object pictures were recorded directly from the exposed left hemisphere of the human cortex at sites whose relation to naming was subsequently established by electrical stimulation mapping. Two simultaneous potential changes are specific to sites where stimulation disrupts naming: slow potentials at premotor sites and focal desynchronization at posterior sites surrounding the Sylvian fissure. These anatomically specific changes are also specific to the task—present with silent naming and absent in a spatial task with the same visual input. Overt speech is also preceded by slow potentials with earliest onset at premotor sites.*

Only certain areas in the dominant cerebral hemisphere are specialized for language, but neurophysiological correlates of language showing intrahemispheric specificity to these areas have not been demonstrated. Such demonstration requires recording from discrete cortical regions, and the pattern of cortical language sites in each subject must be known, as it varies considerably between individuals (*1*). We now report neurophysiological correlates specific to a language task that are also specific to the language cortex. These are changes in event-related potentials (ERP's) during silent naming, recorded from exposed human cortex that was subsequently shown to be specialized for language by the presence of errors in naming when that cortex was electrically stimulated.

These data were obtained from six adult patients undergoing left-hemisphere craniotomies under local anesthesia for resection of epileptic foci (*2*). In all patients, the left hemisphere was dominant for language, as shown by preoperative intracarotid Amytal testing (*3*). After the epileptic focus was identified, 1-mm silver ball electrocorticographic (ECOG) electrodes were placed at eight to ten arbitrarily selected sites generally outside of the epileptic focus, in the cortex surrounding the Sylvian fissure (four patients) or in the frontal lobe (two patients). During ECOG recording, patients engaged in two tasks; (i) name matching, which elicits silent object

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naming; (ii) line matching, which elicits processing of spatial features of the same visual input. Each task was given in separate blocks of trials, each trial consisting of 100-msec exposures of three slides presented consecutively at variable intervals of 4 to 5 seconds. The first slide of each trial was the same in both tasks: an achromatic drawing of a common object with a red line superimposed across it. The second slide in each trial differed for the two tasks. In name matching, it was an achromatic drawing of an object without a line, followed by a third slide, a uniform blue, which cued the patient to state aloud whether the names of the objects in the first two slides (designated O1 and O2) rhymed. The second slide in line matching had only a red line. The third blue slide cued the patient to state aloud whether the orientations of the lines in the first two slides (designated L1 and L2) were the same. Each task was given in blocks, and the patient was informed of the specific task at the onset of each block. Thus, O1 and L1 elicited processing of

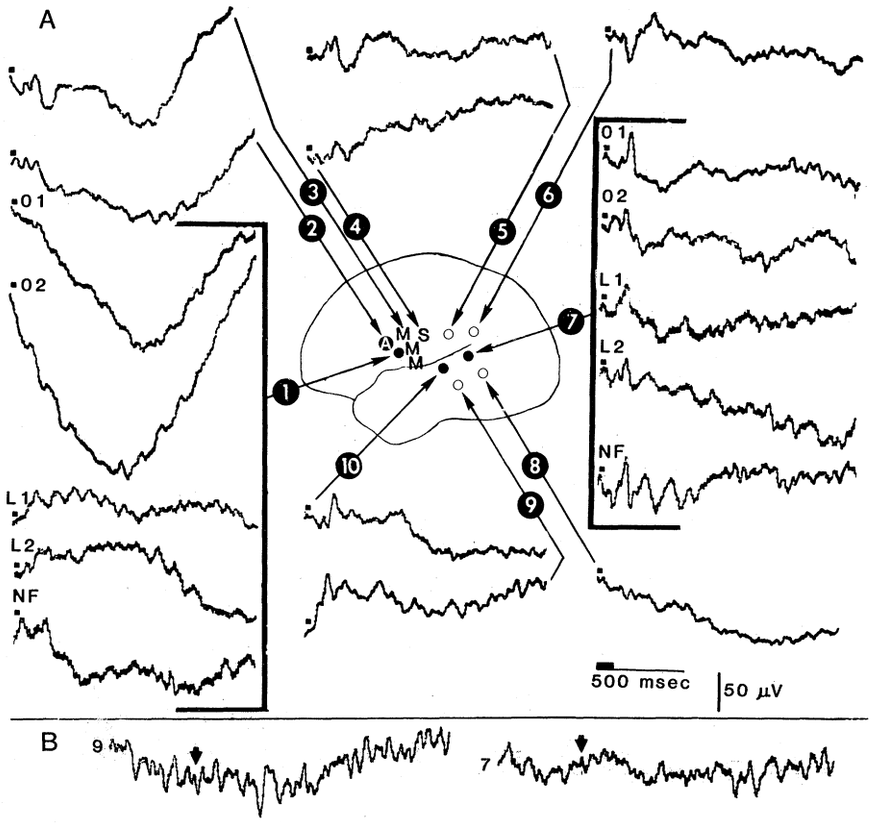

Fig. 1. (A) Event-related potentials after 100-msec flashes of O1, the first silently named object picture in name matching, simultaneously recorded from ten sites in dominant peri-Sylvian cortex of a patient undergoing a craniotomy under local anesthesia. At one posterior site, 7, and one premotor site, 1, ERP's are also shown for the remaining tasks: O2, L1, L2, and NF. Referential ECOG recordings to linked neck reference were amplified by a 16-channel electroencephalograph (Beckman Acutrace) with band-pass of 0.5 to 50 Hz. The electrooculogram was recorded from above the right eye. Tracings are average of 34 trials except for NF (17 samples). Only trials free of response errors, eye movements, or other artifacts are averaged. The digitizing rate was 250 samples per second. Tracings were averaged for 1500 msec after flash onset (small squares). Positive down. Stimulation mapping of these same cortical sites during naming followed these recordings. Results are indicated on the brain map: *M*, facial motor cortex; *S*, sensory cortex. Open circles, sites without naming errors. Filled circles, sites where stimulation produced naming errors without arrest of speech (anomia). At sites 1 and 7, anomia was produced on all three trials with stimulation, at site 10 on only two of three trials. (A) Site where stimulation produced speech arrest on all trials. Error rate on control naming trials without stimulation was zero. Stimulation mapping used 4 msec (peak to peak) biphasic pulses 2.5 msec in total duration at 60 Hz delivered through electrodes separated by 5 mm. The patient is female and has a verbal IQ of 109. Her epileptic focus was confined to the anterior temporal lobe, sparing all ERP recording sites, and was resected after completion of these studies. (B) Single trial recorded simultaneously at sites 7 and 9 for the 500 msec before and 1500 msec after an O1 object picture was presented (onset indicated by arrow). Calibration is as in (A). In contrast to site 9, note the flattening of the tracing at site 7 beginning with the onset of the flash, and the resumption of the high-amplitude oscillations about 900 msec later.

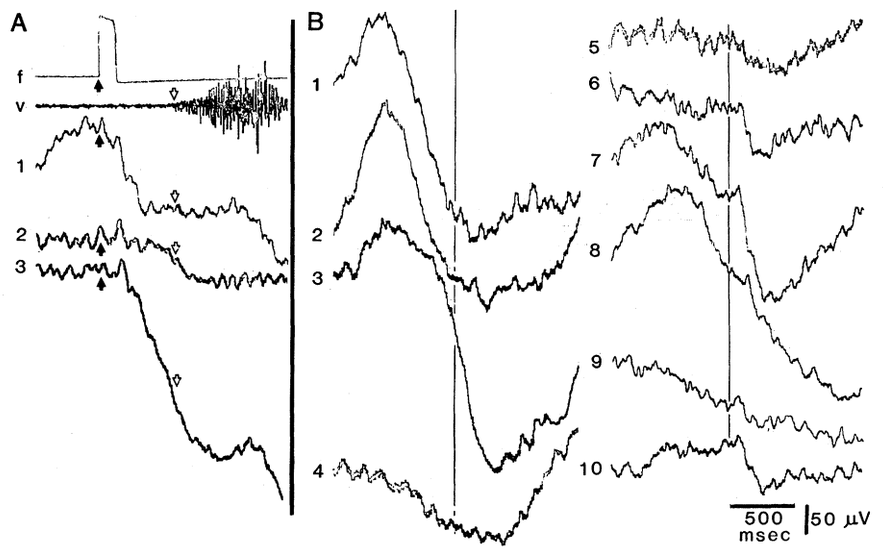

Fig. 2. Event-related potentials related to overt speech, recorded from same sites in the same patient as Fig. 1. (A) Speech cued by blue flash. Abbreviations: *f*, flash; *v*, average of recorded vocalization. Open arrows, onset of the earliest verbal response. Traces shown are averages of 17 samples, 500 msec before and 1500 msec after cue onset (filled arrow). Positive down. (B) Spontaneous "yes." Average of 10 samples of 1000 msec before and after voice onset (vertical line). The positive shift preceding speech is largest at the same sites (1 to 3) showing a positive shift during silent naming. With overt speech, additional positive shifts are also evident at posterior sites (6 to 8, 10) and with spontaneous speech (B) are preceded by a negative wave (sites 1 to 3, 7, and 8); neither feature is seen with silent naming. Averages synchronized with the onset of cued vocalization show an even more distinct onset of the positive shift. In those records, the shift preceding speech occurs earliest at premotor sites, then motor sites, followed by posterior sites.

either a language (O1) or spatial (L1) feature of the same visual input. In this way any ERP changes specific to cortex related to language by stimulation mapping could also be identified as specific to language rather than to spatial processing of the same input. Delaying vocalization to the third cue slide enabled recording of potentials without components related to overt motor speech processes. Cortical potentials were also recorded during 100-msec exposures of clear slides [neutral flashes (NF)] and spontaneous utterances ("yes" and "no"). The ECOG channels, the patient's voice, and a marker for the onset of each flash were recorded on magnetic tape. Off-line analysis included averaging of trials time-locked to the flash onset or the patient's voice.

Immediately after the ERP recording, electrical stimulation mapping of the same cortical sites was carried out for object naming (*1*). Thus, at the completion of the study the relation of a set of cortical sites to object naming had been identified by stimulation-evoked errors, and ERP's during silent naming and during spatial processing of the same visual input had been recorded from the same sites.

Visual inspection of these ERP's demonstrates two changes specific to language-related cortex and to the language task. One is a slow potential occurring at motor and premotor sites (Fig. 1, trace O1, sites 1, 2, and 3). This slow potential is absent at the same sites when the same input is presented in the spatial task (Fig. 1, trace L1, site 1). The potential shift is most prominent in the premotor cortex (Fig. 1, site 1), where it began with the onset of O1 and reached a maximum at about 750 msec. Such potential shifts were evident at this location in five of the six patients. In the two patients with extensive sampling of more anterior frontal sites, these potentials were limited to sites related to naming in the posterior part of the inferior and middle frontal gyri (*4*).

Potential shifts at the same sites were also recorded during cued or spontaneous overt vocalization (Fig. 2). This finding suggests that the potential shift appearing with silent naming is a sign of processing to a stage of subvocalization, inner speech, or effector readiness. A major difference between overt speech and covert naming appears to be the relative involvement of motor and premotor cortex. In the three patients with both motor and premotor recordings, the potential shift was greater in the premotor cortex with silent naming and in the motor cortex with overt speech (mean ratio of motor to premotor positivity; amplitude measured from baseline: 0.74 ± 0.34 for silent naming, 1.93 ± 0.70 for overt speech after the blue cue, and 1.56 ± 0.42 for spontaneous vocalization). These potential shifts began earlier in the premotor cortex (by as much as 100 msec for overt speech after the blue cue), which suggests that premotor areas are involved in an earlier stage of language production than is the motor cortex (*5*). Whether these potentials are unique to the left hemisphere is yet to be determined. We studied one additional patient during the exposure of the right nondominant peri-Sylvian cortex. Similar potentials were recorded from inferior frontal sites preceding overt speech but not preceding silent naming.

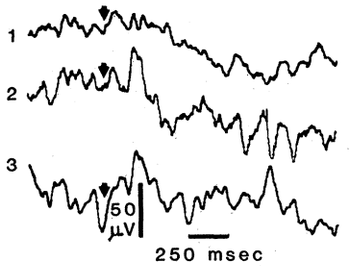

Fig. 3. Event-related potentials following O1 object picture recorded from the dominant peri-Sylvian cortex of another patient. The recording technique is the same as that used in the patient in Fig. 1. Positive down. Arrow indicates flash onset. Responses are averages of 12 trials simultaneously recorded from a parietal site where electrical stimulation uniformly produced anomic errors (site 1), an adjacent parietal site (site 2), and a posterior temporal site (site 3) where electrical stimulation did not alter naming. The female patient has a verbal IQ of 87 and has an anterior temporal lobe focus sparing these recording sites.

A second ERP change specific to silent naming and to the language cortex is seen at posterior sites related by stimulation mapping to object naming. This change appears as a flattening of the ECOG with a suppression of rhythmic activity (Fig. 1, sites 7 and 10). It resembles the desynchronization observed in the electroencephalogram (EEG) in behavioral states associated with arousal. It begins at site 7 after a negative potential with a mean latency of 160 msec that is neither site- nor task-specific to naming (*6*). The desynchronization lasts about 800 msec and is present only during the naming tasks (O1 and O2), not during the spatial tasks (L1 and L2) or in response to the NF's (Fig. 1, site 7). It is not seen in nearby cortical sites unrelated to naming (such as Fig. 1, site 9).

Spectral analysis of the 240- to 960-msec portion of the ERP to O1 and O2 at one posterior site where stimulation disrupted naming on all trials (Fig. 1, site 7), confirms the visual impression, with a marked diminution in power in the 5.56-Hz bandwidth centered at 8.33 Hz compared with all other sites and to spatial (L1 and L2) and NF inputs. This pattern is not evident in the low-frequency (less than 5.56 Hz) range (*7*).

This focal desynchronization could also be identified in single trials (Fig. 1B) and in all patients with exposure of posterior peri-Sylvian cortex (*8*). The results in one patient allow the contrasting of this effect in the peri-Sylvian location with that in a superior temporal gyrus location. In this patient (Fig. 3), naming changes were evoked with stimulation of an inferior parietal site. That site exhibited desynchronization after O1 and O2 inputs, a change that was absent at sites unrelated to naming in the posterior superior temporal gyrus or the adjacent parietal lobe.

Both ERP features that show specificity to a language task and to sites in the language cortex seem to occur in parallel, even though one, the slow potential shift, is recorded from the premotor cortex and the other, desynchronization, from posterior language areas. Both may underlie some of the more widespread changes observed in the scalp EEG during verbal tasks (*9*). Both phenomena suggest focal cortical activation by language stimuli rather than activation of cortex as a whole. Both changes have been related to thalamocortical mechanisms (*10*). Moreover, changes in language behavior thought to represent "specific alerting" to language have been reported with left but not right human thalamic stimulation (*11*). Together, these findings suggest a major role for thalamocortical mechanisms in human language.

ITZHAK FRIED*
GEORGE A. OJEMANN
EBERHARD E. FETZ
Department of Neurological Surgery, University of Washington, Seattle 98195

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2. Five women and one man, 21 to 49 years old (mean, 34.4). The ECOG recording and stimulation mapping during naming to localize the language cortex are essential features of these operations. Procedures used for obtaining informed consent for research conducted during these operations are reviewed annually in advance by the University of Washington Biomedical Sciences Review Committee in accordance with Public Health Service Guidelines for Human Experimentation. Lidocaine or bupivacaine anesthesia were supplemented by intravenous fentanyl and droperidol, 3 to 4 hours before testing. All patients were also on long-term anticonvulsant regimens, most commonly one or more of phenytoin, carbamazepine, valporate, or phenobarbital. Differential effects of

these drugs on ERP's from different cortical sites seems unlikely.
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In one patient, bipolar recordings were obtained between several frontal sites. Similar positive potentials were recorded between a naming-related site in the posterior inferior frontal gyrus and two other sites where stimulation did not disrupt naming. One was in the middle portion of the same gyrus, and another was in the posterior middle frontal gyrus.
Selectively increased activity in the facial motor cortex during overt but not during silent naming has been recorded with regional cerebral blood flow measures also [B. Larsen, E. Skinhøj, N. A. Lassen, *Acta Neurol. Scand. Suppl.* **72**, 6 (1979)].
This nonspecific potential is most prominent at posterior sites, phase-reverses across the Sylvian fissure, and is stable across different stimuli and tasks.
Log spectral density for the 240- to 960-msec interval of the O1 ERP at the 5.56-Hz bandwidth centered at 8.33 Hz at site 7 (the fully anomic posterior site) is 0.81 compared with a range of 1.11 to 1.89 for nonanomic sites. The log values of spectral density at site 7 for the other stimuli are 0.83 for O2, 1.14 for L1, 1.62 for L2, and 1.65 for NF. The coherence between site 7 and the neighboring sites at this frequency is least following O1 and substantially greater for spatial and neutral flash inputs. For example, the coherence (at 8.33 Hz) between sites 7 and 9 is 0.00 for O1, 0.25 for L1, 0.90 for L2, and 0.80 for NF. During silent naming, the activity of cortical region related to naming is differentiated from that of surrounding areas. Spectral analysis performed with SPECTRA [A. Barr, J. Goodknight, J. Sall, J. Helwig, *A User's Guide to SAS* (SAS Institute, Raleigh, 1976)]. Periodiograms were smoothed through the use of an approximate cosine window with 5.56-Hz bandwidth.
In one patient, desynchronization was evident at only one of two posterior sites associated with stimulation-evoked naming changes. In all other patients, such desynchronization was seen at all posterior sites associated with naming changes.
A variety of scalp EEG and ERP changes have been related to language. Often at least one report fails to confirm the finding [S. A. Hillyard and D. L. Woods, in *Handbook of Behavioral Neurobiology*, M. Gazzaniga, Ed. (Plenum, New York, 1979), vol. 2, p. 345; E. Donchin, M. Kutas, G. McCarthy, in *Lateralization in the Nervous System*, S. R. Harnard, R. W. Doty, L. Goldstein, J. Jaynes, G. Kruthamer, Eds. (Academic Press, New York, 1977), p. 330]. Several scalp EEG studies show suppression of 8- to 12-Hz activity during verbal tasks, but anatomic specificity of these studies is limited to the left hemisphere as a whole, and the suppression is not absolute but relative to the right hemisphere. Our findings of a potential shift in premotor and motor cortex preceding the onset of overt speech support the brain origin of similar scalp potentials [D. W. McAdam and H. A. Whitaker, *Science* **172**, 499 (1971)]. However, electromyographic changes preceded voice onset by more than 300 msec [B. Grozinger, H. H. Kornhuber, J. Kriebel, *Prog. Clin. Neurophysiol.* **3**, 87 (1977)]. Thus, although the potential shift preceding overt speech began as early as 680 msec before voice onset in our data, we did not routinely measure the electromyogram, and the onset in relation to speech muscle activity is uncertain. Also, interactions with cerebral respiratory potentials cannot be excluded (Grozinger *et al.*).
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Supported by NIH grant NS 04053. G.A.O. is an affiliate of the Child Development and Mental Retardation Center, University of Washington. E.E.F. is affiliated with the Department of Physiology and Biophysics and the Regional Primate Center, University of Washington. We thank A. B. Scheibel, A. Forsythe, and T. Thrall from the University of California, Los Angeles, and W. H. Calvin, C. B. Dodrill, A. R. Wyler, E. Lettich, and D. F. Kalk from the University of Washington for advice and assistance.
Present address: Department of Psychology, University of California, Los Angeles 90024.

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Circadian Variation in the Latency of Brainstem Responses and Its Relation to Body Temperature

Abstract. *The auditory brainstem response varies in a circadian rhythm that is negatively correlated with the circadian rhythm in oral temperature. The auditory brainstem responses and oral temperature were recorded every 3 hours from three healthy male subjects during a 2-day period. The data indicate that a reduction of 1°C in oral temperature is associated with an increase of 200 microseconds in the latency of wave V of the auditory brainstem response, and of 160 microseconds in the interval between waves I and V.*

Auditory brainstem responses (ABR's) are widely used for diagnostic purposes by neurologists and audiologists (*1*). The ABR's, first described by Jewett *et al.* (*2*), consist of five to seven waves (numbered I to VII) elicited in the brainstem by clicks presented in rapid succession. The ABR's are extracted by averaging signals from scalp recordings of the electroencephalogram. Although the origins of the potentials are not fully understood (*3*), the first five waves appear to be associated with neural activity at, or near, the first five relays in the auditory pathway (*4*). In persons with normal hearing the ABR's are remarkably stable and the latencies of the waves, particularly waves I, III, and V, are consistent across individuals (*5*). Latency deviations and, less often, amplitude deviations can indicate pathology in the auditory system (*6*). We present data suggesting that at least a portion of this variation in latency is related to the circadian rhythmicity of body temperature (*7*).

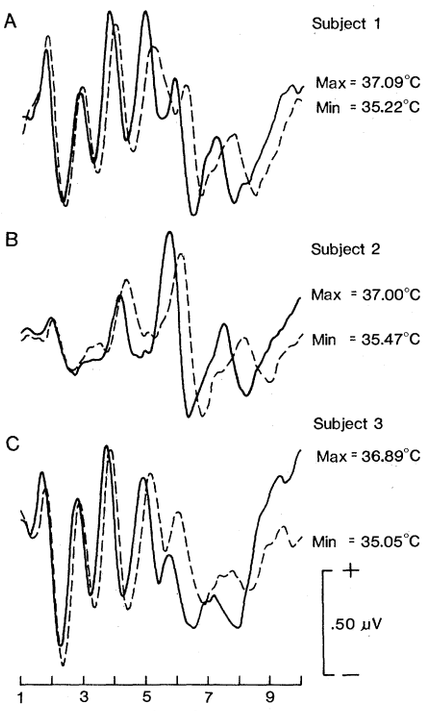

Fig. 1. Auditory brainstem responses recorded at the vertex in response to 4000 0.1-msec clicks, from each of three subjects at 65-dB hearing level. Solid lines represent ABR recorded when the subject's oral temperature was at a maximum in the experimental period; the dashed line was recorded when oral temperature was at a minimum. Positivity at the vertex relative to the mastoid is indicated by an upward deflection.

Several investigators have asserted that the latencies of the ABR's, particularly of wave V, increase with decreasing body temperature. They based their assertions on observations in nonhuman species where body temperature was changed artificially (*8, 9*), or on temperature measures taken from patients who were, for one reason or another, hypothermic (*10*). We report here that naturally occurring circadian variations in body temperature are correlated with similar changes in the latency of the ABR's.

Oral temperature and ABR's were recorded every 3 hours during a 51- to 54-hour period for a total of 17 recording sessions from each of three healthy male undergraduates (mean age, 20 years) who were paid for their participation. The initial recording session began at 1200, 1300, and 1400 hours (central standard time) and ended 2 days later at 1200, 1600, and 1400 hours for subjects 1, 2 and 3, respectively (*11*). The subjects were free to come and go during the day but slept overnight in the laboratory. They reported that they slept during most, if not all, of the recording sessions (*12*).

The EEG was recorded from a silver–silver chloride scalp electrode placed at the vertex (Cz) and referred to the mastoid process of the right ear. Subjects were grounded at the forehead. The vertex and reference electrodes were affixed with collodion. The short-stem scalp electrodes were placed on the subject before the first session and then reapplied after the seventh recording session. The ground electrode was reapplied every session. Electrode impedance was maintained well below 3 kilohms. The signals were amplified by Grass P511J amplifiers, set to a bandwidth of 100 to

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