

Systematics of the Evoked Somatosensory Cortical Potential

Abstract: This paper presents the results of a series of experimental studies in which a digital computer averaging technique was used to explore the dynamics of the electric response of the human somatosensory cortex evoked by pulse electrical stimulation of nerves in the wrist.

A nomenclature is presented for the typical components of the complex waveform which the authors consider to be representative of the evoked potential. The effects of stimulus amplitude, bilateral and bitemporal stimulation, and sleep on the evoked corticogram were investigated. Psychophysical studies were also carried out which complemented the evoked potential studies, and comparisons were made between the neurological and psychological data.

Introduction

The recent decade of neurophysiological research has seen the development of a new trend in studies of organic communication and data processing systems. The accumulated body of knowledge of single-cell physiology and of the action of synapses now allows us to approach, in a meaningful fashion, the problems of the complex interactions of many cells. This new work is of significance to psychologists because of the current interest in the neurophysiological foundations of behavior. Enough progress has been made to show that some problems, particularly those of sensation, can be attacked at the present time. Hartline's studies of the limulus eye¹ are a classic example of neuronal explanations of complex behavior from which indirect comparisons may be made to human perceptual problems.

Stimulation of the somatosensory system with pulse electrical stimuli produces a compound action potential which is the result of synchronized nerve cell activity in the cortex. Since these potentials are very small and are mixed with electroencephalographic and electromyographic activity, it is necessary to average many successive responses to detect and measure the stable evoked waveform. A general-purpose digital computer can be used to accomplish this statistical detection.

This paper will discuss the results of a series of such experiments now being carried out at the biophysics laboratory at the Thomas J. Watson Research Center, which investigates the systematics of the cortical potential

evoked by stimulation of peripheral nerves and recorded from surface electrodes placed on the scalp over the somatosensory region of the human brain.

Earlier studies at this laboratory²⁻⁴ have dealt with temporal and spatial coding of nerve impulses in the peripheral nerves of man. The positive correlations found between these nerve impulses and the subjects' reports have led us to carry out further studies while recording from the somatosensory cortex. In this paper the stimuli have been directly compared with the peripheral nerve response, the evoked cortical potential and the psychophysical response.

Dawson⁵ had originally proposed the application of radar averaging techniques to the detection of evoked potentials from the human somatosensory cortex. Because of other physiological and electronic noises, the small evoked potentials are not easily seen in single records. The signal-to-noise ratio is at least as bad as one part in ten, in many instances, and it is clear that when the simple detection of the responses is so difficult, satisfactory quantitative measurements are even more difficult. By reiterative photography the detection of the larger components was made possible, and Dawson's earliest work used multi-exposed photographic records to detect the responses. Dawson⁶ later went on to develop an electromechanical commutator system which produced a summated measure of the response by filling a bank of capacitors to voltage levels proportional to the total

amount of activity at a given set of delays. Since the noise tended to diminish in amplitude relative to the repetitive portions of the signal, the effective signal-to-noise ratio increased rapidly. Since 1950, several other investigators have engineered new devices to accomplish this averaging function. Davis and Ferris⁷ and Rosenblith,⁸ have reported on recent work in this field. Particular attention should be paid to the well-known work⁹ on auditory problems at the Research Laboratory of Electronics of MIT (where W. A. Clark, Jr.¹⁰ first implemented a digital computer averaging technique when he constructed the ARC-1 special purpose device) and the work of B. S. Rosner, et al.¹¹

The present studies were carried out to determine which measures of the evoked cortical responses could be correlated with behavioral measures and, therefore, were representative codes of psychological phenomena. Because of certain features of the recorded potentials it was also possible to tentatively associate certain portions of the averaged waveform with specific anatomic structures. Section A of our *Experiments and results* section presents a description of the waveform which, along with the results of Section E, the effects of sleep on the evoked potential, contribute to this association. Section B presents the results of a neurophysiological study of the relation between the amplitude of the evoked potentials and stimulus intensity, and mentions the conflict between these data and those from psychophysical experiments in which subjective magnitudes were measured. Section C presents the results of studies of temporal and spatial interactions, while Section D provides the psychophysical data for spatial interaction in an analogous experiment. In this way we have approached our goal of directly comparing the behavioral and the electrical data.

Subjects

A wide variation in the waveform of the evoked potential is evident in different subjects, independent of recording technique. We have found, for example, that there was a wide range of response amplitudes ranging from unmeasurably small to signals that are visible in single oscilloscope traces. Wide individual differences between subjects also occurred in the shape of the response. *Based on our sampling and on the published records of Dawson, we have decided to study a response type in which all of the components are present and well enough resolved to be independently measured.* On this basis we selected two subjects who exhibited this optimal waveform and have carried out the majority of the work to be reported here on these two young college men. The psychophysical study of spatial interaction (Section D) was, however, performed with two male and two female subjects recruited from a nearby college.

Instrumentation

The electronic system used in this work consists of two independent functional units. The first is designed to produce highly regulated, constant-current, voltage-isolated electrical pulses to be used for stimulating nerves.

The second is designed for amplifying and recording data in both analog and digital form for computer entry.

• Stimulation system

The stimulation system will not be treated in detail in this paper. A complete description of the circuitry involved in pulse electrical stimulation of human peripheral nerves has been reported by Uttal.¹² Figure 1 is a block diagram of the experimental system as it is currently organized. A preset counter controls the presentation of a specific number of stimuli through any one of three channels. A master clock pulse initiates a delay time base from the delay generator. At any time, chosen by settings on the front panel of the instruments, any of the pulse formers can emit a pulse which times and shapes the stimulus. These pulses, however, are not adequate for percutaneous stimulation because of the capacitive impedances of the skin which distort the current waveform so much that an accurate measurement of stimulus intensity is not possible. To achieve a constant-current waveform, isolated from ground, the voltage pulse is fed into a power amplifier and then to a rf isolator unit. This unit not only reduces stimulus artifact but also serves as a safety feature for the subject. The output of the isolator is then fed into the constant-current unit. Stimuli generated by a selected combination of the three stimulator channels were then communicated to a selected electrode position through a routing panel. Stimuli were usually 0.5 msec in duration and a level was chosen between 0 and 10 ma, constant current, through the underlying tissue.

In these studies of human somatic sensation the stimulus electrodes were placed over a superficial portion of the median nerve at the wrist. The electrodes were hemispherical stainless steel buttons 3/16 of an inch in diameter.

The subject's hand (or hands, in the bilateral interaction studies) was immobilized by a plaster cast to avoid movements of the electrode or nerve relative to each other. Electrode location had been shown to be critical in an earlier study from this laboratory (Brown¹³).

The subject was seated in a shielded enclosure and actively observed, on a monitoring oscilloscope, the electrical potentials picked up from the electrodes on his scalp. In this manner the background electroencephalographic activity was reduced by his very attentiveness and the subject was also able to monitor and reduce electromyographic activity.

Pulse electrical stimuli were chosen because they approximate the critical time dimensions of the actual nerve-action potential. Thus, we are able to use a large fund of knowledge of axonal physiology, much of which is based on responses following impulse stimulation.

• Data recording system¹⁴

In these studies of evoked potentials from the human somatosensory cortex, potentials were picked up by button electrodes held by a special framework on the head. A reference electrode was centered on the forehead. The

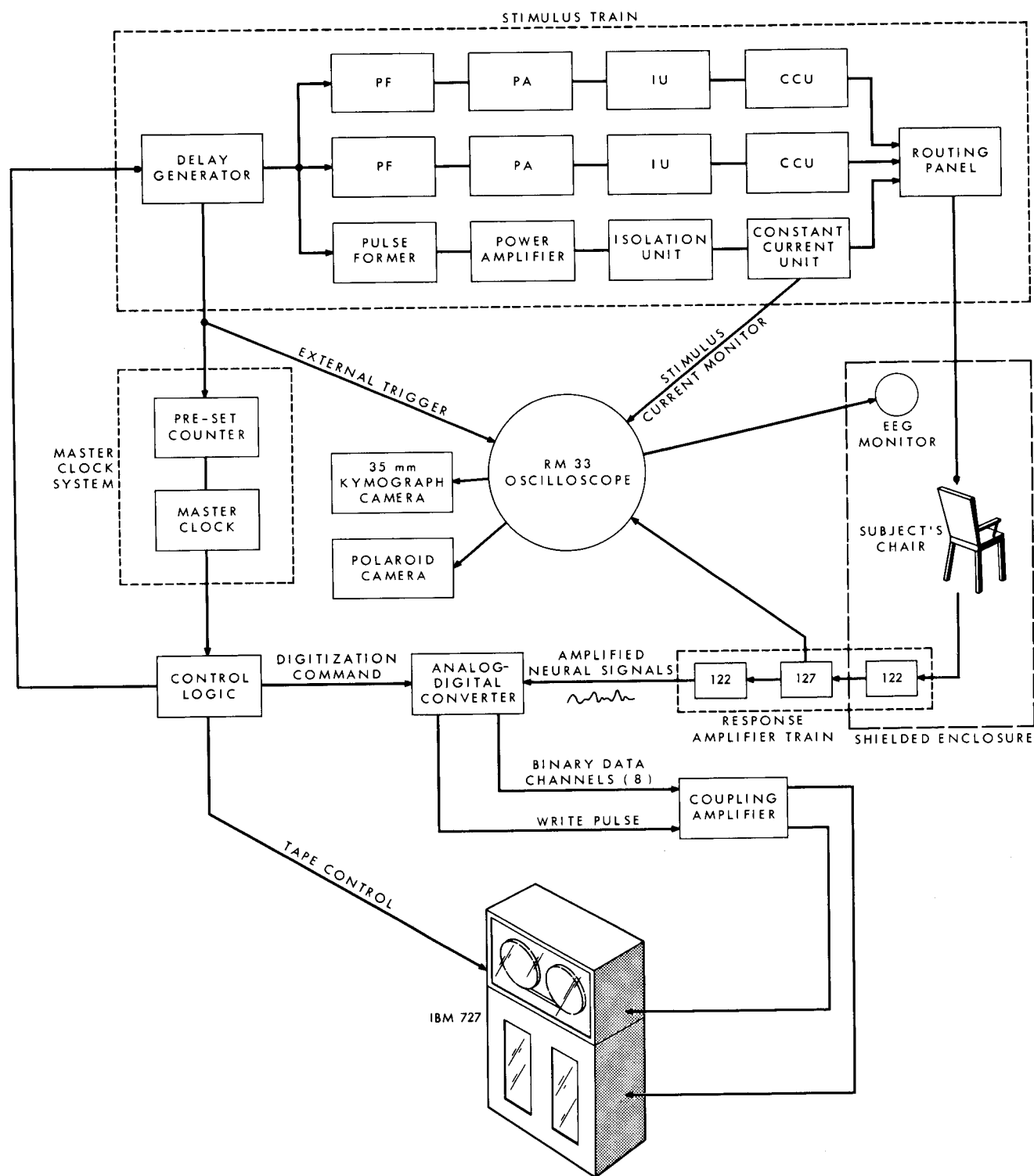


Figure 1 The experimental arrangement, showing the role of the digital data recording system.

active electrode was usually placed over the postcentral somatosensory area, contralateral to the stimulated arm but in some experiments were placed over the corresponding ipsilateral region.

Figure 1 also shows the data analysis system. The

analog signal representing the voltage picked up from the subject was connected through high-gain amplifiers to the input of an analog-to-digital converter. The converter sampled the data and 12,000 times a second converted the analog voltage into a six-bit binary code. The

conversion rate and the length of the interval during which conversions were carried out were under the direct command of the control logic system. In addition to these control functions, the control logic also operated an IBM 727 digital tape recorder which had been specially modified to accept the data from the analog-to-digital converter.

The control unit may be operated in one of two modes. In the first, a "manual continuous" control starts the tape in motion and then after the appropriate delay commences the coding conversions. The tape drive and the converter then remain active until the switch is returned to its normal position. In this mode, data may be digitized and recorded from a continuous analog signal for long periods of time.

In the second mode, a master clock emits a pulse which initiates a sequence of control signals that start the tape, command digitization, and stop the tape after a length of time that is predetermined by the operator. In this latter mode a single tape record representing a period of time following a specific event, such as the presentation of a stimulus, can be recorded. Thus, data representing a number of sequential responses may be recorded for later processing on a standard computer.

It was in this latter mode that the data recording system was used in the present series of experiments. All of the evoked potentials we report and analyze are, in fact, averages of 80 sequential 320 msec records presented at $2\frac{1}{2}$ sec intervals. Experimental runs usually lasted from 1 to $1\frac{1}{2}$ hr including subject preparation time.

The digital tape records were processed on an IBM

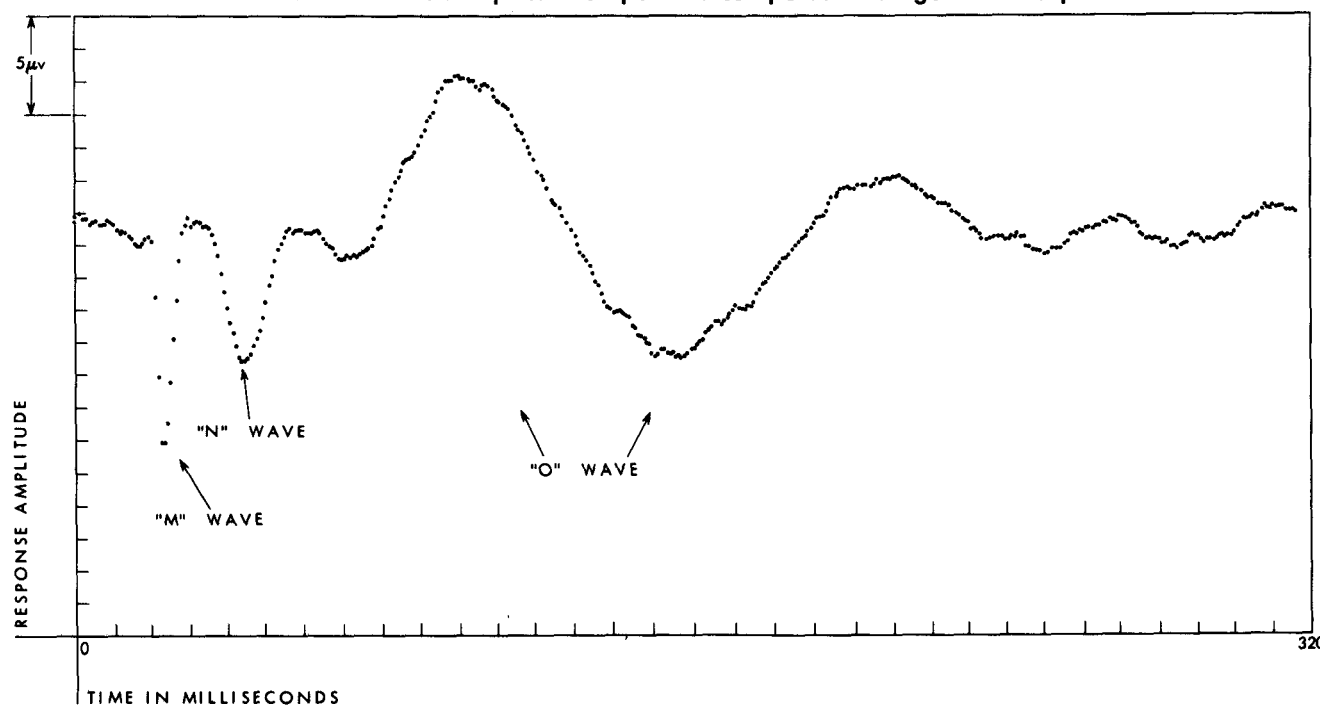
Research 704 computer and were edited so that only every tenth point was used in the calculations. Since the sampling rate was 12 kc/sec, each data point was separated from its neighbors by 0.8 msec. Averaging was accomplished by computing the arithmetic mean of the 80 values of the digitized signal at each of these 400 successive sample times. The computer then punched a set of cards upon which these 400 individual time averages were tabulated. These cards were then listed and plotted by means of a point plotter driven by a modified card reader. It is important to distinguish between two kinds of variance in our data. The first kind is due to the extreme signal-to-noise condition found in this type of recording and is characterized by extremely large variations in the sequential samples. The second is the variance of the *averaged* data which was well within acceptable limits for each subject.

Experiments and results

A. General waveform and components of evoked cortical potential

Figure 2 is a typical averaged response of the somatosensory cortical potential evoked by a 5 ma, constant-current pulse stimulation of the median nerve at the contralateral wrist. The response is seen to be composed of three main components which we have named the *M*, *N*, and *O* waves. (Our polarity convention is that a positive potential at the active electrode is indicated as a *downward* deflection on our graphs.)

Figure 2 A typical averaged evoked cortical potential from the somatosensory region showing the *M*, *N*, and *O* waveforms (320 msec sample). Each point is computed average of 80 responses.



The *M* and *N* waves are positive spikes lasting for 9.6 and 19.2 msec respectively for subject J.W., and 6.4 and 16.0 msec respectively for subject J.L. The *M* wave was larger than the *N* wave for J.W. but smaller than the *N* wave for J.L. The *M* and *N* voltage waves could be detected mainly on the rear quadrant of the head contralateral to the stimulated nerve except for a very small ipsilateral deflection caused, we feel, by passive spread of current.

The *O* wave, for our two subjects, was a long, slow negative excursion followed by a similar positive excursion and then a small negative one. All three excursions were of widely varying latency and amplitude. The duration of one cycle of the *O* waveform was approximately 100 msec and it did seem to be associated with the state of alertness of the subject. These latter two conditions suggest that the *O* wave is in some way related to the well-known alpha rhythm, which is recorded without specific external stimuli. We observed that it is nonspecific in origin and recordable over the entire head. These results corroborate the findings of Larsson.¹⁵

Other smaller or less specific peaks were irregularly noted but these seemed most often to be manifestations of the leading or trailing edges of the three major features.

The most significant difference between subjects detected during our pilot studies was the fact that with certain subjects the *M* and *N* waves seemed to be partly or even wholly fused. Figure 3 shows the range of *M* and *N* waveform types recorded. The reason for these individual differences is unknown at this time. It is clear, however, from our pilot studies that it is not a function of the electrode placement, since deliberate variations in electrode location did not substantially change the waveform characteristic for a given subject.

The *M* and *N* waves also differed in the variations in recorded latency. The latency of the *M* wave was fairly stable, varying by only ± 1 msec for constant stimulus amplitude. The *N* wave, however, exhibited more jitter in the averaged responses, displaying recorded ranges as great as ± 4 msec. The variability of the latency of the specific peaks of the *O* wave is considerably wider than that of either of the two primary spikes. The first negative peak of the *O* wave occurred over a range of 88 to 135 msec following the stimulus. The latency of the positive peak ranged from 135 to 200 msec and the third smaller negative wave could be found peaked between 209 and 385 msec after stimulation. It should be reiterated that the *O* wave variability was very large. The *O* wave seemed to be related to extremely complex phenomena such as awareness, attentiveness and thought, as one would expect from a process associated with the alpha rhythm.

B. Evoked potential as a function of stimulus amplitude

As mentioned previously one of our immediate goals is a fourway comparison between the stimulus, the peripheral nerve response, the evoked brain potential and the subjective response. In earlier studies,^{4, 13} we had demon-

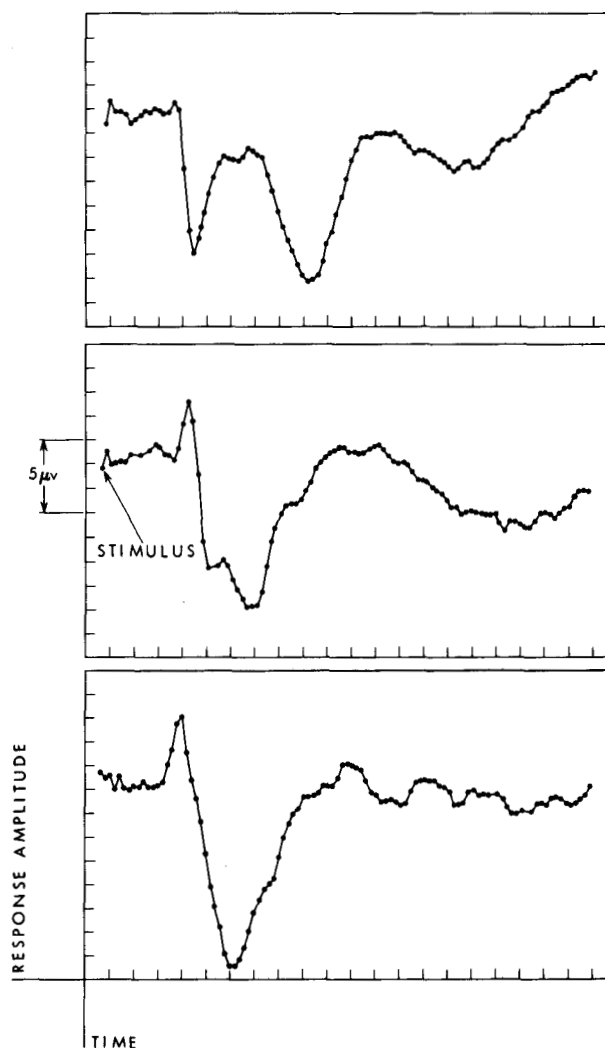


Figure 3 Averaged evoked cortical waveforms from three different subjects showing the range of individual differences recorded in the *M* and *N* waves. (100 msec sample)

strated the high correlation between the stimulus and both the peripheral nerve responses and the subjective magnitude estimates. In the present work it was desired to detect and measure the brain potential while varying the stimulus amplitude.

Pieron,¹⁶ among others, has speculated that the central coding of sensory magnitudes is a function of the number of central neuronal units which are activated upon receipt of a transmitted signal from the periphery. This would suggest that a larger stimulus amplitude would evoke a larger cortical response voltage as more and more cells were recruited.

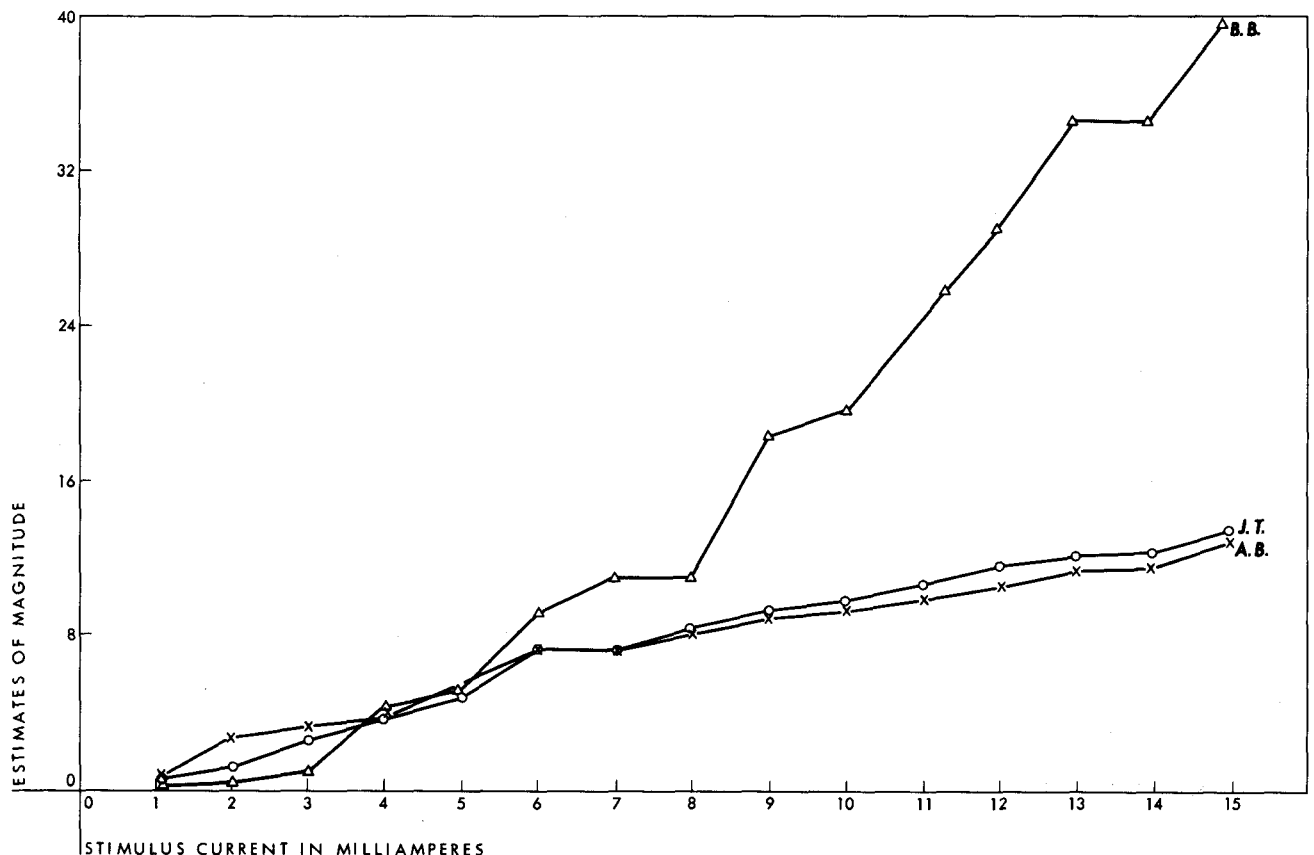
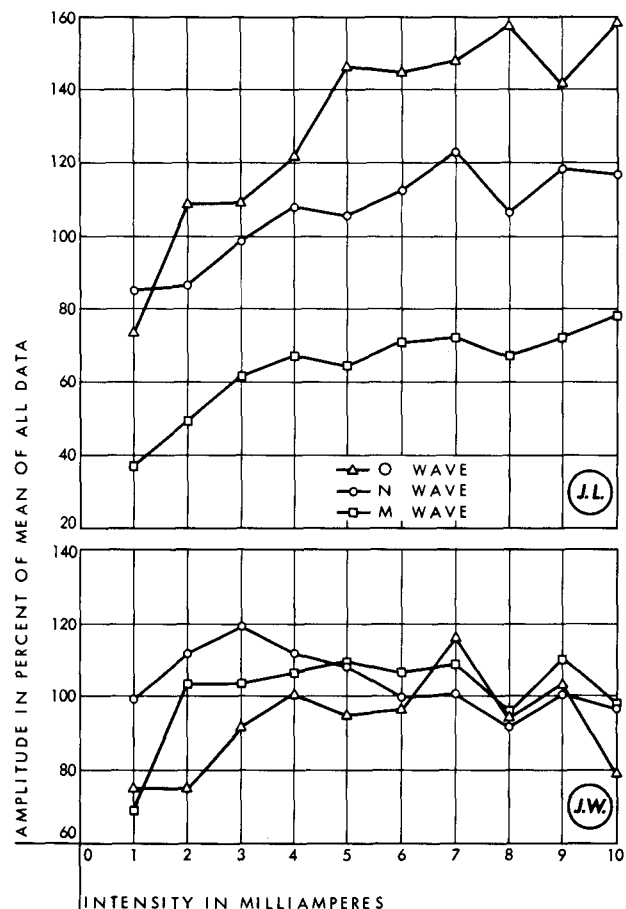
Our experiments were designed to determine the functional relationship between the amplitude of constant current pulses and the amplitude of the various identifiable components of the cortical response.

Figure 4 The amplitude of the M, N, and O wave-
forms for the two subjects as a function
of stimulus current level showing the un-
usually large amplitudes of the recorded
potentials for low levels of stimulus in-
tensity. Each point is average of 400
records. Data are normalized as described
in the text.

Stimuli ranging from zero to ten ma in one-ma steps were presented in a constrained random order (random selection without replacement until each stimulus level had been presented once). Each session produced average responsive curves for 10 different stimulus intensities. The amplitudes of the M, N, and O waves were then determined from the averaged records. For this purpose data from five separate sessions are pooled together and shown in Fig. 4. The data for each subject are normalized as a percentage of the mean of all data for the three waves.

The anticipated relationship between stimulus and amplitude of cortical response was not observed. The cortical response, rather than being barely detectable at levels near psychophysical threshold and increasing with increasing stimulus magnitude,¹⁷ is well over half of the maximum amplitude at threshold (~1 ma) and is nearly

Figure 5 Psychophysical estimates of magnitude
made by three subjects to stimuli of ran-
domly ordered magnitude.



100% long before full stimulus amplitudes are reached. This "saturation" phenomena in man was anticipated by a recent study of Mark and Steiner¹⁸ which showed the relation between the cat's somatosensory cortical response and the peripheral nerve response to be of this same form — nearly total evoked brain potential at low levels of peripheral nerve response.

The intriguing comparisons are: 1) that the estimates of magnitude made by the subjects to randomly presented pulse stimuli amplitudes (as shown in Fig. 5) did show a monotonic increase in the perceived sensation over the full range of stimuli; and 2) the peripheral nerve response has also been shown by Brown¹³ to increase monotonically as a function of stimulus amplitude to levels well above 10 ma.

C. Studies of spatial and temporal interactions between evoked potentials

In order to investigate further the dynamics of the evoked potential and to seek information concerning the organization of cerebral interconnections, we have turned to studies of interactions among temporally or spatially separated stimulus inputs.

Two separate studies were carried out. The first dealt with the responses produced by presenting separate and isolated electrical pulse stimuli to the median nerves on both the left and right wrists. The delay between the ipsilateral and contralateral stimuli was varied in this study. Three hourly sessions were carried out to explore the conditions in which the contralateral stimulus led the ipsilateral and three separate sessions were carried out to determine the results for those conditions in which the ipsilateral stimulus led the contralateral. Since each condition was based upon a computer average of 80 records, each point on Fig. 6 represents the average of 240 records. Within each session the conditions representing variations in the lead time were presented in a constrained random order to minimize sequence effects.

The second experiment dealt with the responses generated by stimulation with two temporally separated electrical pulses applied to the same electrode on the contralateral wrist. The effect of a preceding stimulus on the magnitudes of the *M* and *N* waves produced by a second stimulus was determined in this experiment. The time intervals between the two stimuli were again varied by presentation without replacement and 80 records were averaged to produce an average response record. Thus each point plotted in Fig. 7 represents the average of 480 separate stimulations (six sessions).

In the first experiment, the results obtained (see Fig. 6) indicated that there was only a minimal detectable inhibitory interaction between evoked potentials produced by stimuli applied to the left and right arms respectively. By stimulating the contralateral median nerve alone with a 5 ma current a control response level was established. An equal-amplitude stimulus was then applied to the ipsilateral median nerve and either followed or led the contralateral stimulus by time intervals varying between plus and minus 100 msec. Figure 6 shows that the re-

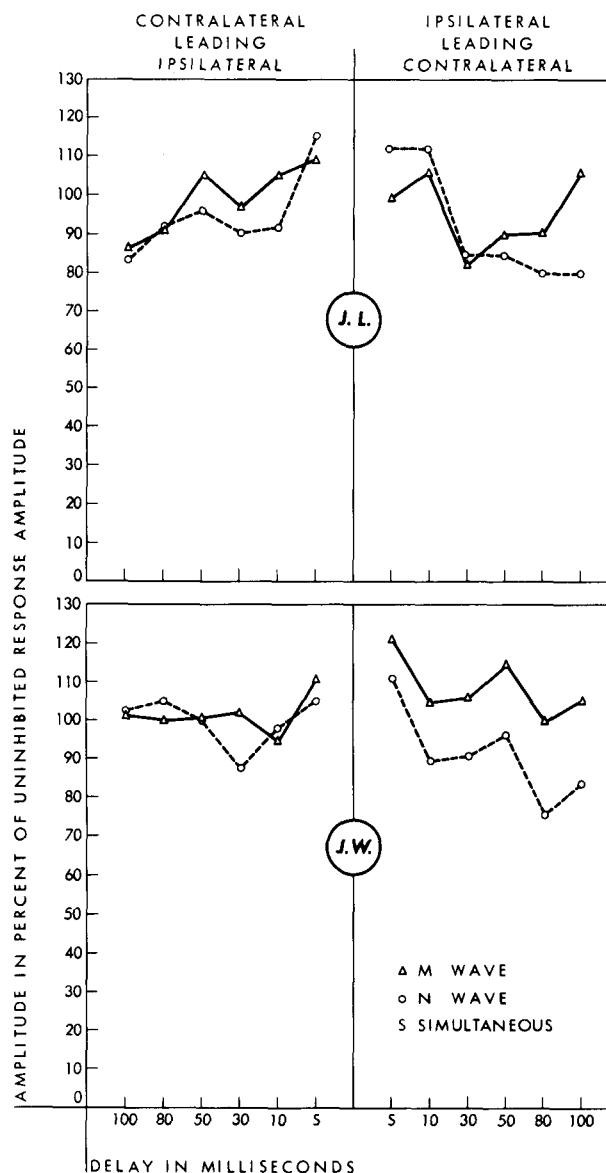


Figure 6 The amplitude of the contralateral *M* and *N* waves as a function of a leading or lagging ipsilateral stimulus showing the absence of any significant interaction. Each point is average of 240 records.

sponse amplitudes do not change appreciably as a function of the ipsilateral stimulation. The slight amount of change in no way corresponds to the complete blocking of the contralateral response by the ipsilateral as reported by Nakahama¹⁹ in the cat. In this Figure, the points representing the results of simultaneous stimulation do appear to be greater in magnitude than the control signals. Occasionally a small *M* and *N* wave can be detected on the ipsilateral side of the body. Since the time dimensions are exactly that of the contralateral *M* and *N* wave it is felt that this represents a passive spread of the potentials through or along the surface of the skull. The increase in

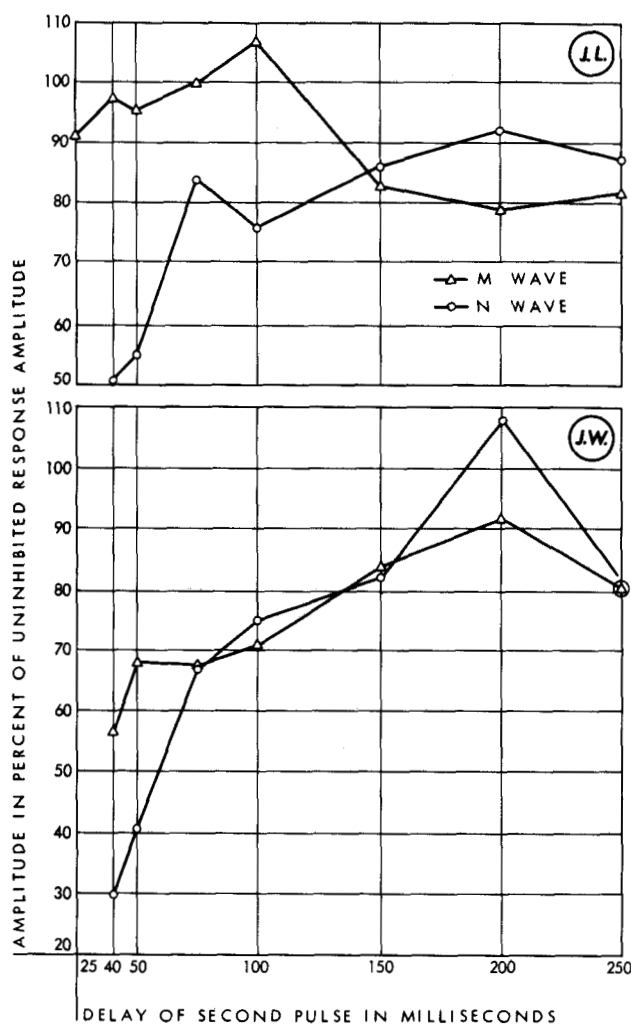


Figure 7 The amplitude of the *M* and *N* wave produced by a second stimulus as a function of the interval between the first and second stimuli showing the evoked potential refractory effect.

the response magnitude for simultaneous stimulation is, therefore, due to the addition of the small *M* and *N* potentials from the other side of the head.

In the second experiment in which two stimuli, delayed in time, were applied to the same electrode on the contralateral arm, we were able to study the "refractory" function for the evoked potential. In this case, however, a considerable amount of interaction did occur, as shown in Fig. 7. It was demonstrated that the effects of a preceding stimulus on a later one were very much like the results obtained from the stimulation of single fibers in that a refractory period was present, but that it extended over a much longer period of time. The inhibitory effects of the first stimulus on the last appear to affect the *M* wave less seriously than the *N* wave. The response pattern for this experiment did differ between the two subjects. Both subjects showed that the inhibitory effects of the first

stimulus lasted up to 200 msec and both showed that the *M* wave was less seriously affected than the *N* wave. It is also clear, however, that the *M* wave of J.L. was not affected by the first stimulus. At this time we can only point out that the absolute magnitudes of J.L.'s responses were somewhat less than those of J.W., the reason for the difference in *M* wave inhibition being obscure.

In addition to demonstrating the refractory period of larger systems of neurons, this experiment also acted as a control to show that differences in response amplitude are detectable by our measurement techniques.

D. Psychophysical study of spatial interaction

A study of spatial interactions among electrical stimuli to the fingers has also been carried out that is directly relevant to the evoked potential studies reported in the previous section.

The stimulation devices utilized in this experiment were essentially the same as those described earlier. Two identical channels conducted electrical pulses which were 0.5 msec in duration and were selected between 0 and 4 ma to the fingers.

The neurophysiological recording system was not used in this experiment, but rather the responses recorded were threshold determinations verbally reported by the subjects.

The independent variable of this experiment was spatial position, i.e., the fingers, to which masking and the test stimuli were routed. This routing was accomplished by an automatic switching device that utilized the duplicate station of an IBM 526 summary card punch to set the states of two independent relay trees. Data were recorded by keypunching the threshold level onto other regions of the same prepunched cards which contained the stimulus configuration. Complete details of this dual use of the summary punch are available elsewhere.²⁰

Dime-size stainless steel electrodes were attached to the index and middle fingers of both hands. No preparation other than washing the hands was deemed necessary because of the constant-current characteristics of the stimulator.

The effects of a relatively strong masking stimulus, presented to one finger, on the detection threshold of another electrical stimulus, presented to a different finger, were measured. Three types of stimuli configurations were used: (a) unmasked test configurations, to determine the base level, (b) four ipsilateral masking configurations, and (c) eight contralateral masking configurations. These configurations are listed as the horizontal coordinates in the four graphs in Fig. 8.

Ninety-six of these three types of stimuli configurations, dispersed in the same constrained random order, were presented in one-hour sessions each day for 10 days. Each stimulus was preceded by a red signal light.

While the masking current pulse was held constant at 4 ma, the experimenter manually manipulated and presented to the subject an ascending series of the test pulse in 0.1 ma steps between 0 and 1.6 ma and 0.2 ma steps above 1.6 ma. An ascending series was terminated when the subject responded with the correct number or num-

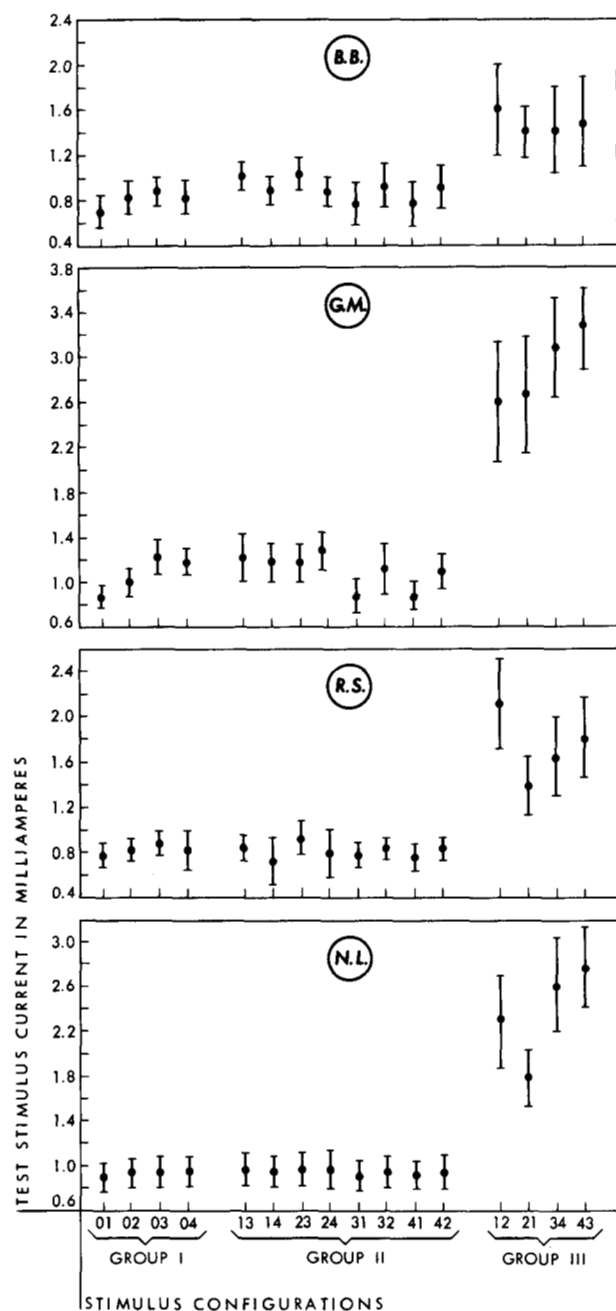


Figure 8 The results of the psychophysical study showing the absence of significant bilateral interaction and the presence of an ipsilateral elevation of the threshold.

bers. The subjects were allowed to respond only with the word "nothing" or the code numbers of either the one or two fingers in which they felt the masking and test stimuli. The experimenter keypunched the test current level into the keyboard on the summary punch, thus recording the threshold level and resetting the relay trees for the next configuration, when the subject first reported both test and masking stimuli to be present.

The test stimulus followed the masking stimulus by 0.5 msec to reduce electrical interaction in the isolation units and a configuration was presented every 5 to 10 sec.

The results of this investigation of contralateral interaction are depicted in Fig. 8. On the charts of this Figure the vertical coordinates are measured in milliamperes required for threshold detection. The 16 experimental configurations are each represented by a pair of numbers. The first digit indicates the finger to which the masking stimulus was presented (a zero indicating no masking), and the second digit specifies the test finger. Each finger represents the mean of 60 threshold determinations and the bars indicate the standard deviations.

It is clear that little, if any, difference exists between the unmasked and contralaterally masked thresholds but that a substantial inhibitory interaction occurs between two stimuli presented to the same hand. The details of this ipsilateral interaction are discussed in an earlier paper.³

Although the experiments are not exactly analogous, since we are stimulating the skin of a finger rather than a large nerve trunk and determining threshold rather than response amplitudes, this comparison of ipsilateral and contralateral psychophysical interaction does support the results of the studies of interaction in evoked brain potentials. Strong interactions occur when both the masking and test stimuli are presented to the same side of the body and there is little indication of interaction when they are presented to opposite sides of the body. The reader's attention is also directed to a study of temporal interaction by Schmid which augments the results of this study of spatial interaction by exploring the effects of variations in time delay between the masking and test stimuli. This is described in Rosner's recent work²¹ on peripheral nerve action potential comparisons with psychophysical results.

E. Effect of sleep

The effect of sleep on the evoked somatosensory potential was determined by carrying out two separate sets of recording sessions in which records were gathered under both sleep and awake conditions. In the first set of sessions, the stimulating electrodes were fixed on the contralateral arm, while during the second set of sessions the responses were generated by ipsilateral stimulation.

The results of these experiments are characterized by the records shown in Fig. 9. The contralateral stimulation produced the usual strong *M*, *N*, and *O* waveforms. The ipsilateral stimulation, on the other hand, produced only the nonspecific *O* wave, as described earlier in this paper. When the subject is asleep a surprisingly small change occurs in the contralaterally generated *M* and *N* waveforms, for it is only in the trailing edge of the *N* wave that any change can be detected. This is manifested as a much slower rise time, or a broadening of the base of the *N* wave in such a way that it merges directly into the first negative-going portion of the *O* waveform.

This change in the trailing edge of the *N* wave may be due to either one of two different causes, since we are recording a weighted algebraic summation of the various

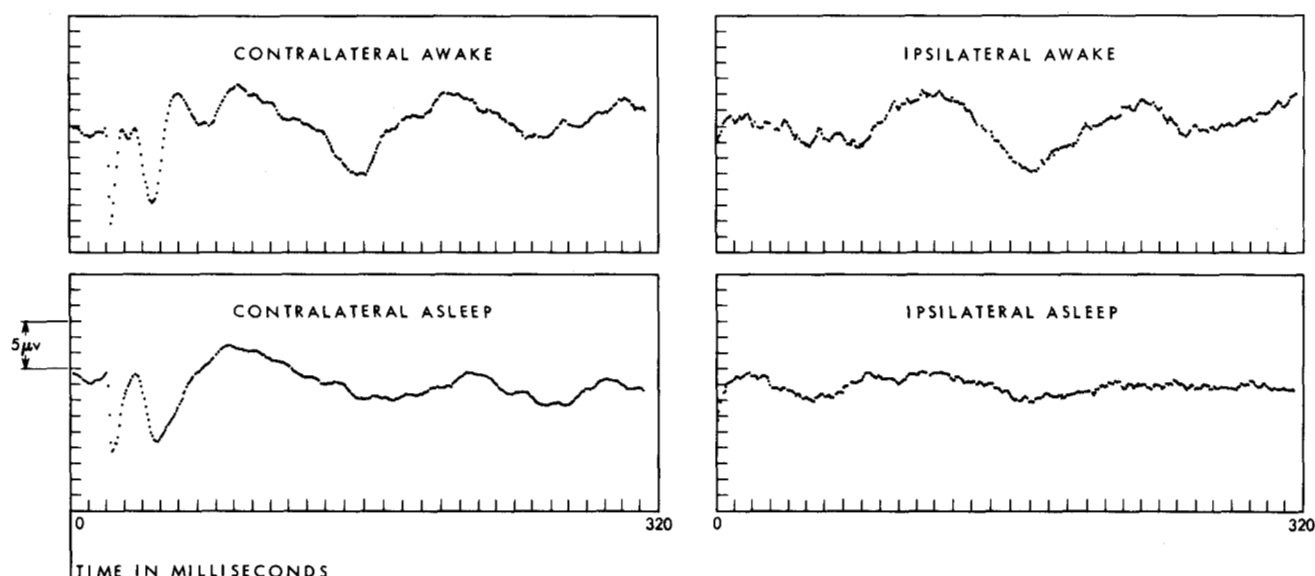


Figure 9 The effects of sleep on the averaged evoked potential showing the change in the trailing edge of the *N* wave and the decrease in amplitude of the *O* wave when the subject is asleep.

potentials. It might be that the *N* wave itself is changing in shape, but it may also be that a positive deflection is developing at the leading edge of the *O* wave. We are able to discriminate between these two alternatives because the *O* wave exists independently on the ipsilateral side of the body. It is clearly shown in the ipsilateral records that the *O* wave decreases in magnitude as the subject falls asleep. A comparison with the contralateral evoked potential confirms that this is also happening on the contralateral side of the body, and we may, therefore, conclude that the change in slope of the *N* wave is, indeed, a change in the *N* wave itself and not an artifact of recording both *N* and *O* waves simultaneously.

We may summarize the results of this study of sleep and wakefulness by concluding, first, that the nonspecific *O* wave behaves very much like the classical reticular activation response, decreasing in magnitude as the subject goes to sleep. The relationship between this correlation and the previously mentioned similarities of the alpha rhythm and the *O* wave will be discussed later.

Discussion

At the beginning of this discussion it is important to point out that electrophysiologists are bound to a limited number of neurophysiological techniques. When recording from the intact human body we may for the most part record only voltages which are classified as *compound action potentials*. Thus in studies of human neurophysiology we find reports on the massively synchronized electrical fields recorded by the electroencephalographer or the electrocardiographer. Compound action potentials, of course, do not completely define the neural activity. The somatosensory potential evoked by a massive electrical shock is a highly "nonphysiological" condition and

there is, at present, some question as to whether the somesthetic sensory system responds similarly under more usual stimulus conditions. Furthermore, recording through the skull introduces uncertainty about the localization of the source of the potentials because they occur equally over rather large portions of the head. We appreciate these difficulties and call them to the reader's attention. However, the problem of decoding the neural language of human sensation (as in any translation problem) can be solved only by comparing neurophysiological and psychological data recorded under conditions as nearly identical as possible.

• Identification of the components

The basic waveform recorded in these experiments obviously indicates that we are dealing with a complex response. The evoked potential is not only the summation of many thousands of neuronal potentials but also appears to be the summated responses of several major neurological systems. The *M*, *N*, and *O* waves probably reflect the responses of three separate afferent systems, and it is possible to suggest associations with anatomical structures although, admittedly, this must be done with a great deal of caution. The anatomy of the complicated pathways of the neurological structures subserving the somatosensory modalities are not completely understood and most related physiological and psychological experiments contain inconsistencies and ambiguities. Of the three waveforms shown here, the most positive identification that can be made is the *O* waveform.

The brain stem *reticular formation* has been thought to be a system responsive to inputs from many different sensory modalities. Its output has generally been described as nonspecific because, instead of projecting to

specific cortical sensory areas, stimulation of the reticular formation activates the entire brain to a greater or lesser amount. Generally these nonspecific activations have been reflected in the ordinary electroencephalogram and appeared to produce the same changes as produced by variations in wakefulness. Moruzzi and Magoun²² have shown that high levels of reticular stimulation produced an "alert" pattern, while a minimal pattern of stimulation produced a "sleep" pattern. Both the EEG and the ascending reticular formation were characterized by the following set of properties:

1. Bilaterality of response
2. Long latencies
3. 100 msec fundamental wavelength
4. Wide variability with subjective state
5. Diminution with sleep
6. Widely diffused response in time.

Upon comparison with the *O* wave characteristics obtained in the present studies, the set of qualities enumerated above characterize this portion of the evoked potential also. It is therefore suggested that the major system contributing to the *O* wave is the reticular activation system.

The *M* and *N* wave, on the other hand, are characterized by:

1. Contralaterality of response
2. Short latency
3. High reliability
4. Durations of 6 to 10 msec
5. Localization over the post central somatosensory cortical region
6. Relative independence of subject's state of consciousness.

These characteristics correlate with the comparable measures of potentials evoked from the sensory areas of the cortex and recorded with electrodes placed directly on the brain. Rose and Mountcastle,²³ in a comprehensive review of present knowledge of the somatosensory system, describe the two major pathways which convey information to the cortex — the medial lemniscal and the spinothalamic systems. Although, as they point out, a great deal of uncertainty exists about the exact anatomical and physiological organization of these two systems, it is well established that the medial lemniscal system projects "at least to Somatosensory Area I" in a topologically organized fashion. The spinothalamic system is known to project "at least to Somatosensory Area II" and to be composed of smaller fibers than those found in the medial lemniscal pathways.

The spinothalamic system is also believed to have ipsilateral components, although the current consensus of opinion assumes that the medial lemniscal pathways all cross to the contralateral side of the body. As Rose and Mountcastle put it, "It is tempting to assume that the second somatic area is activated solely by the spinothalamic system . . ." To us, it is even more tempting to suggest that the *M* and *N* waves may represent the actions of

these two major pathways and that all functional differences between the two waves are due to this difference in locale and their respective transmission rates. The greater sensitivity of the *N* wave to two-pulse stimulation, as seen in the studies reported here, further suggests a smaller fiber system and certainly one that is separate from that mediating the *M* wave.

● *The saturation phenomenon*

As mentioned earlier, Mark and Steiner¹⁸ have observed the saturation phenomenon in direct comparisons between the peripheral nerve action potential and the evoked cortical potential in the cat. Their results showed, interestingly enough, the same range of variability of the degree of saturation as displayed by our two subjects. The adaptive value of the saturation phenomenon to the organism seems to lie in the nervous system's ability to amplify signals from the periphery in such a way that the signal level at the cortex is well above the spontaneous "noise level." Thus any suprathreshold signal, no matter how small, would be capable of initiating the sequence of events leading to a perceptual or even a motor response.

The mechanism for the production of the saturated responses depends upon dispersion of the input signals in both time and space.

Wall,²⁴ by means of a novel recording technique, has shown the dispersion in time taking place in second-order neurons in the dorsal column of the cat's spinal cord. Single-spike potentials in the peripheral nerves gave rise to continued trains of potentials in these second-order neurons. Wall concludes that these repetitive firings are due to the interaction of these cells with other interconnected units in a reverberative circuit. Thus, this mechanism acts as an amplifier by increasing the number of spike potentials generated by a single afferent input. The response is diffused in time and presumably also in space. At the cortex we see the ultimate effects of this amplification at each successive synapse. The duration of the cortical response is upwards of 300 msec and obviously an extremely large number of cells are activated by near-threshold responses.

Experiments of this sort provide a possible explanation for the saturation effect and, though we may speculate upon its adaptive value, we are still left with the problem of explaining the coding of sensory intensity. As mentioned above, our psychophysical measurements clearly show that the amplitude of the sensation increase throughout the entire 10 ma range of stimuli. Experiments by Brown¹³ from this laboratory further show that the peripheral nerve action potential also increases throughout that 10 ma range.

Two possibilities are suggested to explain this coding dilemma. It may be that the amplitude of the response is not truly indicative of the number of responding cells. Spread of response to include more cellular units for increased stimulus strength is a well-known phenomenon of evoked potentials. Indeed, cortical localization is defined in terms of "centers of activity" and the spatial

range of this activity depends upon the stimulus amplitude. This spread of response might not be reflected in our amplitude measures.

The second escape from this dilemma may be that, in fact, the number of cells responding is not the critical coding dimension. Some subtle spatial coding is certainly possible in which either different regions or different configurations of cells become active. If this is the case, then, although there is no question of the true neural origin of these evoked responses, they may represent an epiphenomenon other than the true information transaction with which we are concerned.

• *Bilaterality in brains of cat and man*

Our experiments in contralateral interaction, with both neurophysiological and psychophysical indicants, agree that there is no significant interaction between responses produced by independent stimuli applied simultaneously to each hand. Furthermore, our evoked potential studies have not shown any ipsilateral components of the *M* and *N* wave which can be clearly associated with the primary somatosensory projection pathways. Such findings suggest cortical organization in man in which there is a high degree of independence between the two cerebral hemispheres. It is well known that this is the case: Surgical transection of the *corpus callosum* reported by Akelaitis,²⁵ seems to have little behavioral effects, and Glees and Wall²⁶ discuss the absence of communications between the halves of the human thalamus.

Penfield and Rasmussen's studies²⁷ on the exposed human cortex have shown that the facial region alone is bilaterally represented in Somatosensory Area I. Other than this one region, no other evidence of bilaterality in Somatosensory Area I was found. The human Somatosensory Area II also proved to be a region of contralateral representation contrary to the usually accepted notion. The one possible exception to this generalization is the face, but the second facial region lies contiguous to the first and responses are difficult to resolve in that area.

In the cat, however, the extensive researches of Nakahama^{19, 28, 29} indicate a different situation. Nakahama studied the interconnectivity of the cat's cortical layers in two ways. In the first he stimulated the cortex in one region and studied the evocation pattern in other regions of the cortex. Secondly, he stimulated various combinations of peripheral nerves both ipsilateral and contralateral to the cortical area in which he was recording. Using these methods he demonstrated connection patterns between ipsilateral Somatic Area I and II. Grafstein³⁰ has also shown the connectivity between the contralateral corresponding areas in the cat. Nakahama's interaction studies showed further that there was functional interaction between the afferent pathways since both contralateral and ipsilateral stimulation inhibited responses in both Somatic Area I and II.

Though the details are still not complete, the general picture of human cortical bilaterality is now beginning to clarify. There is, as one ascends the phylogenetic tree, an increasing tendency towards encephalization and then

subsequently towards a functional separateness of the two halves of the brain. In the cat a high degree of interconnectivity occurs between the four somatosensory regions. In man, the two somatosensory areas on either side of the brain appear to be relatively independent.

Summary

1. The evoked somatosensory potential was studied by an averaging technique and, although reliable results were recorded from individuals, wide ranges of individual differences were found among the various subjects studied.

2. A response type was selected in which all components were present and sufficiently resolved to be independently measured. This typical evoked potential was a combination of what appears to be three basic waveforms which we have called *M*, *N*, and *O* waves.

3. A "saturation" phenomenon was discovered which complicated the issue of the coding of sensory intensity when these results were compared to analogous psychophysical data.

4. Sequential interactions from temporally separated ipsilateral stimuli were shown to exist in the form of an extended refractory period.

5. No interaction could be detected between stimuli presented to opposite sides of the body.

6. Psychological studies confirmed that there was no interaction between stimuli presented to opposite sides of the body.

7. Sleep was shown to affect the *M* and *N* waves in only trivial ways, while the *O* wave was completely abolished by sleep.

8. As usual, the exploration of this new area has led to many unanswered questions. The preliminary nature of our results and the limitations of the evoked potential technique emphasizes the large amount of research which is yet to be done in this area.

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Added in proof:

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