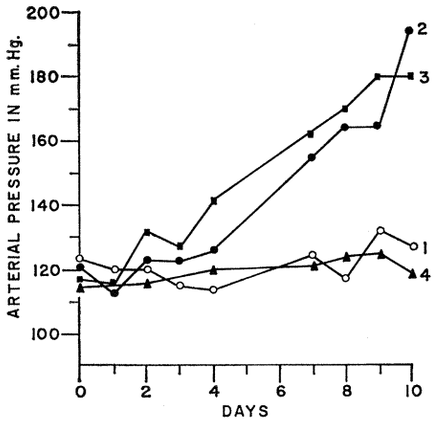

Fig. 1. Curves of the blood pressure of rats injected with extracts of rat kidneys (curve 1), rat renin (curve 2), rat renin and extracts of rat kidneys (curve 3), and saline (curve 4).

tion (*10*). Similarly, we found a decrease in the renin content of the remaining kidneys of uninephrectomized rats treated with renin and an increase in the width of the zona glomerulosa of the adrenals, which is the generally accepted site of aldosterone synthesis.

Evidently, homologous renin reproduced the effects of the endocrine secretions of clipped kidneys, thus eliminating the need to postulate the existence of another renal factor. Although the renin preparation was crude, it is likely that renin and not impurities were responsible for the effects described since treatment with angiotensin can also elicit sustained elevation of blood pressure accompanied by inhibition of renin formation and stimulation of aldosterone release (*11*). The amounts of renin administered may appear enormous when compared with the intravenous dose necessary to produce a similar acute pressor effect; however, presumably only an infinitesimal part reaches the blood stream, since no increase in blood pressure was detected before the 4th day.

The acute pressor activity which follows intravenous administration might best explain the development of hypertension after prolonged treatment. All the evidence indicates a more complex mechanism. Indeed, one point common to this type of experiment with renin or angiotensin (*11*, *12*) is the delayed appearance of hypertension. This latent period suggests that a critical amount of pressor material should accumulate before it raises arterial pressure by direct effect on the vascular system. This is unlikely because of the short half-life of angiotensin of less than 30 minutes (*13*) and the abrupt fall in pressure on cessation of angiotensin infusion (*12*). As an alternative, the existence of secondary mechanisms which may be nervous or endocrine has to be considered. One possible nervous mechanism is based on the ability of angiotensin to intensify normal neurogenic vasomotor activity (*14*). It has also been proposed (*12*) that angiotensin may cause specific cerebral vasoconstriction, which would in turn alter the activity of medullary vasoconstrictor centers.

The endocrine effects of angiotensin are better documented. Administration of renin, or angiotensin, in subpressor doses stimulates specifically aldosterone secretion; clinical and experimental renal hypertension are associated with aldosteronemia; aldosterone causes hypertension; administration of renin to aldosterone-treated rats precipitates a syndrome reminiscent of malignant hypertension (*15*). There is, however, no evidence that during the prehypertensive phase the renin-angiotensin-aldosterone system is activated to the point of being a determining factor in the evolution of hypertension. Hypertension probably cannot be explained according to a single scheme; each of these mechanisms may participate from the beginning, acting either together or in succession, and in the course of hypertension one of them may become predominant.

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20 May 1964

Attention, Vigilance, and Cortical Evoked-Potentials in Humans

Abstract. *Computer-averaged potentials evoked from the cortex were recorded to nonsignal stimuli and to randomly interspersed signal stimuli requiring detection and response during prolonged visual vigilance. As detection efficiency diminished over time, the amplitude of evoked responses to nonsignal stimuli decreased and latency increased. Fluctuations in vigilance (attentiveness) during the course of the task also were accompanied by corresponding changes in evoked-potentials to nonsignal stimuli. More specific lapses of attention, revealed by detection failures, resulted in average evoked-responses of lower amplitude to missed as compared with detected signals.*

Recent research has been focused on possible neural mechanisms mediating fluctuations in attentiveness. Several reports have dealt with changes in evoked-responses to sensory stimuli during attentive and inattentive states (*1*). Most of this work has been conducted with animals, although there have been a few reports of experiments carried out with human subjects (*2*). Thus far, the results have been largely inconclusive, due, we believe, to methods of varying and measuring attentiveness.

One area of psychological investigation which has been intensively concerned with short- and long-term fluctuations of attention is that dealing with performance on "vigilance tasks" (*3*). Most workers in this field agree that failures in signal detection and the long-term decrement and fluctuations in performance that characterize such tasks can be attributed to changes in the observer's state of attentiveness. Accordingly, the experiment described herein was designed for investigating changes in the potentials evoked from the human cortex averaged during a vigilance task requiring visual discrimi-

nation and response. Detection performance was used as a behavioral measure of attention and inattention.

A vigilance task lasting 80 to 100 minutes was performed on five occasions by each of three subjects. The task required a key-pressing response to dim flashes (signals) aperiodically interspersed among more numerous brighter flashes (neutral, nonsignal stimuli) requiring no response. The light flashes were produced by two Grass PS-1 photostimulators set at intensity 4, and diffused through an opal glass bowl upon a 10 × 12-cm flashed-opal glass screen located at the end of a viewing tube 30 cm from the subject's eyes. Flashes occurred at a rate of one every 3 seconds; non-signal flashes had a luminance value of 15 lam and signal flashes were approximately 0.2 log units dimmer with luminance of 9 lam (*4*).

The electroencephalogram was recorded from the scalp over the right occipital cortex with a Grass model VI electroencephalograph, the electrode being sited approximately 2.5 cm above the inion and 2.5 cm to the right of the midline (O_2). The other electrode was over the midline vertex (C_z). Evoked-responses to the flash stimuli were recorded on a frequency-modulated tape recorder, and time-averaging was accomplished by a Mnemotron computer of average transients, since regular electroencephalographic recordings do not reveal the minute responses to individual flashes. Eye movements were also recorded for control purposes.

During each 5-minute period of the task 100 bright (nonsignal) and 10 dim (signal) stimuli were presented. This enabled computation of two kinds of average evoked-potentials. Averages of responses to the 100 nonsignal stimuli presented during each successive 5-minute period of the task provided data corresponding to fluctuations in observing-behavior or attentiveness and to overall decrement in vigilance. Evoked-responses to signal stimuli, separately computed according to whether or not the subject correctly detected each signal, provided data corresponding to specific attention and inattention to these stimuli, as defined by detection behavior.

The evoked-potentials to flash stimuli which are recorded from the human scalp typically consist of complex series of waves. In this experiment the principal identifiable component of the response was a prominent negative wave with peak latency of about 160 msec. For purposes of quantitative analysis of the evoked-potentials, the amplitude (trough-peak-trough) and latency of this peak were measured.

Characteristic of performance in vigilance tasks of the type used here is a decline in detection efficiency with time. In this experiment the combined data show that the percentage of signals correctly detected in each 5-minute period of the task declined from a mean of about 80 percent at the beginning to about 50 percent at the end. During the same time the amplitude of the average evoked-responses to nonsignal stimuli decreased from a mean of about 13 to 10 μv, and the mean latency increased from approximately 155 to 165 msec. The rank-order correlation between the percentage of correct detections and the evoked-potential amplitude was + 0.75, and that between percentage correct and evoked-potential latency was −0.75.

Figure 1 illustrates typical experimental sessions for two subjects, P.N. and M.H. Each trace shows the average evoked-potentials to 100 nonsignal stimuli presented during each 5-minute period of the task. The column to the right shows the percentage of correct detections of signal stimuli which were randomly interspersed during the same time period. During most experimental sessions, there was an overall progressive decline in the amplitude and an increase in the peak-latency of the principal component of the average evoked-response and a corresponding reduction in the percentage of signals correctly detected. This result is shown clearly for subject P.N., but is less marked for subject M.H. whose performance in the vigilance task was very stable during this session.

In addition to these overall trends showing a correspondence between vigilance decrement and evoked-potentials, there were briefer concurrent fluctuations in detection performance and evoked-potentials which were very pronounced in some experimental sessions. For example, Fig. 1 shows that in the 5-minute period 9 for subject P.N. and the 5-minute period 11 for subject M.H., low performance efficiency was associated with relatively low amplitude of the evoked-potentials. Frequently, in adjacent 5-minute periods there were contrasting increases in amplitude of

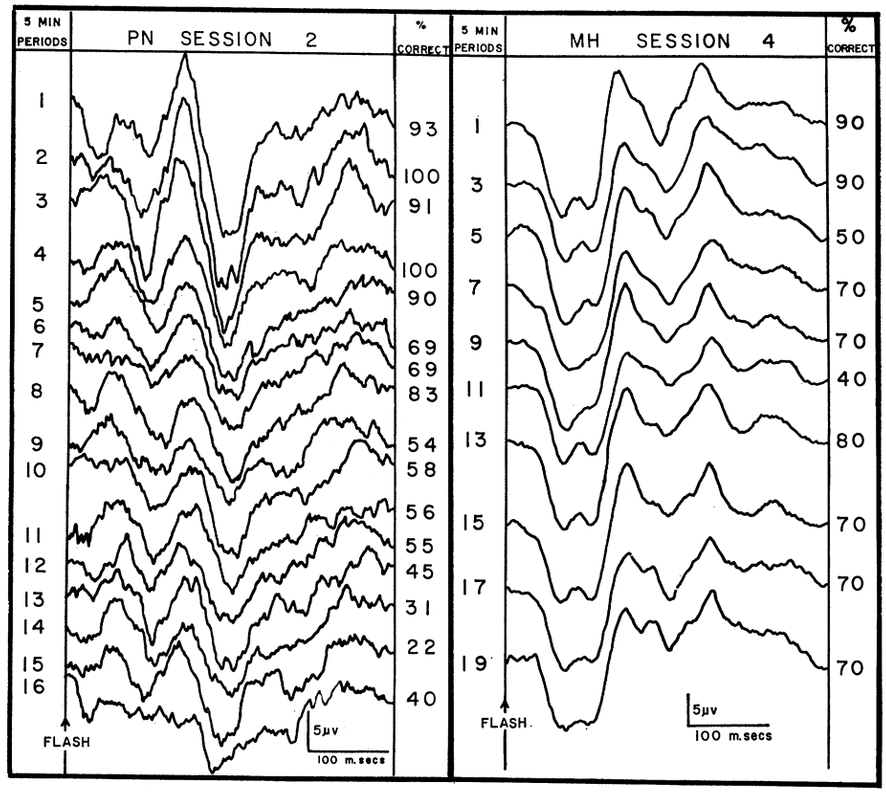

Fig. 1. Computer-averaged evoked-potentials for 100 nonsignal stimuli presented during successive 5-minute periods of a visual vigilance task, together with the percentages of randomly interspersed signal stimuli correctly detected during the same time periods. Recordings: occipital to vertex reference; negativity upward. Subjects P.N. and M.H.

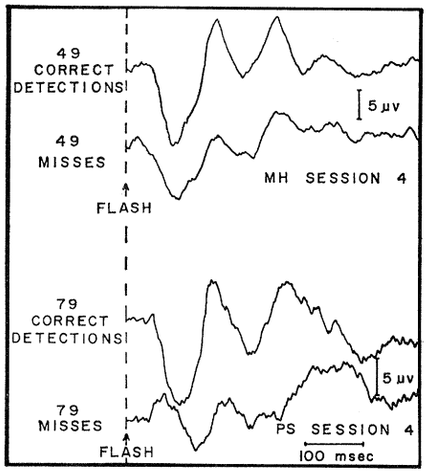

Fig. 2. Computer-averaged evoked-potentials for equal numbers of detected and missed signal stimuli by subjects M.H. and P.S. Both subjects show evoked-responses of reduced amplitude to the missed signals.

evoked-potentials and performance efficiency. These relatively short-term fluctuations in detection performance and in evoked-potentials to nonsignal stimuli appear to reflect changes in the subject's attentive state.

Heretofore the average evoked-potentials were computed for nonsignal stimuli only and reflect long-term changes in vigilance and shorter-term fluctuations in attentiveness. To focus upon a more specific aspect of attention pertaining to the detection of specific signal stimuli, average evoked-responses to signal stimuli were separately computed for signals which were correctly detected, and for those which were not detected, thus contrasting attentive and non-attentive conditions. Figure 2 shows clearly the differences between the evoked-potentials under these two conditions. The evoked-responses to signals which a subject failed to detect (misses) during an experiment were typically reduced in amplitude as compared with those of an equal number of signals which were correctly detected. These differences between detected and missed signals were equally marked during both early and late stages of the experimental task, thus showing that the differences were not dependent upon the general decline of vigilance. In all 15 experiments the differences were in the same direction; however, the magnitude of the differences varied considerably.

These results indicate that reduced attentiveness, as measured objectively by signal detection in a vigilance task, is paralleled by corresponding reductions in amplitude of visual, cortical evoked-potentials in humans. Although this experiment did not deal specifically with the related question of whether enhanced attentiveness increases the amplitude of the evoked potential, results obtained by Davis (*5*) in an auditory discrimination situation indicate that this may be the case.

In vigilance research many workers have long been aware of the need for an independent measure of observing-behavior (attentive states) during those periods of the task when signal stimuli are not presented. The evoked-potential data for the nonsignal stimuli indicate that as vigilance, defined by detection performance, fluctuated and declined during the course of the task, there were corresponding changes in the evoked-potentials to these stimuli. Thus, changes in the amplitude and latency of the evoked-potentials to non-signal stimuli may serve as a direct measure of observing-behavior in vigilance tasks of this type. Additionally, evoked-potentials averaged separately for specific signals to which the subject is instructed to respond, and to which he may or may not respond, provide a measure of fluctuations in focal attentiveness.

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24 April 1964

Enhancement of Evoked Cortical Potentials in Humans Related to a Task Requiring a Decision

Abstract. *The averaged, slow response evoked by auditory stimuli and recorded from the vertex of the human skull can usually be enhanced by requiring the listener to make a rather difficult auditory discrimination. An easy routine reaction is not effective.*

An electroencephalographic response to auditory, visual or tactile stimuli (*1*) can readily be recorded from the vertex of the human skull by means of an average response computer. The response is polyphasic, with a well-marked negative peak at about 100 msec (for auditory stimuli) and a positive peak at about 175 msec.

Actually this slow evoked response, from 50 to 500 msec after the stimulus, is very complex. We think we can recognize at least four components which overlap more or less and which may vary independently both across subjects and across conditions. Analysis of these wave forms will be presented elsewhere, but a useful approximate measure is the peak-to-peak voltage from the (largest) negative peak at about 100 msec to the (largest) positive peak between 150 and 200 msec (*2*).

The slow response in question must not be confused with earlier evoked responses, at 50 msec or less, which are chiefly muscular in origin (*3*). The latter are best recorded near the inion or over the temporalis muscle and are increased by increase of resting muscular tone. Our slow responses are best recorded from the vertex, which is remote from major muscles, or from more frontal areas and they are unaffected by changes in muscular tone. Their slow time course and very long recovery period are hardly compatible with a muscular origin. On the other hand, the slow evoked responses do not originate in the primary auditory area. They arise diffusely from the cortex near the top and front of the head and they are not specific to any one sensory modality.

The amplitude of the various slow waves varies not only with the intensity of, and the intervals between, the stimuli but with the individual subject, his state of arousal, the novelty of the stimulus, and other experimental conditions. This average response varies considerably from run to run, but it is