from baseline cardiovascular levels under the same general laboratory conditions obtaining for the four baboons which provide the basis for this report.

The results of this experiment show clearly that instrumental learning of cardiovascular responses can produce sustained large-magnitude changes in blood pressure which cannot be accounted for on the basis of short-term "voluntary mediators" (for example, the Valsalva maneuver) (*3*). All four baboons in this study showed daily elevations of 30 mm-Hg or more in both systolic and diastolic blood pressures and maintained such elevations for the entire 12-hour conditioning-on segment of each experimental session. These findings suggest the involvement of more durable adaptive mechanisms supporting the sustained pressure elevations, although the relative contributions of cardiac output and peripheral resistance to the establishment and maintenance of these hypertensive levels cannot be determined from the present data alone. In dogs anticipating (over a 15-hour interval) performance on a shock-avoidance procedure (*13*), and in rhesus monkeys during a 72-hour shock-avoidance procedure (*14*), similar blood pressure elevations have been reported, and concurrent measurements of cardiac output under such conditions (*15*) have revealed that the pressure elevations were determined by substantial increases in total peripheral resistance. Although the relationship of these sustained blood pressure elevations in the baboon to the circulatory changes characteristic of essential hypertension in humans (*16*) is far from clear, chronic exposure to aversive behavioral conditioning procedures has been reported to produce hypertensive patterns (*17*), with a bradycardia accompanying the chronic pressure elevations in at least some animals (*18*). The present findings with the baboon extend the range of potentially useful laboratory models for the analysis of environmental-behavioral influences upon the cardiovascular system, and call for further experimental scrutiny of the physiological mechanisms (for example, baroreceptor reflex) which mediate this significant alteration of the systemic circulation.

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Electrical Signs of Selective Attention in the Human Brain

Abstract. *Auditory evoked potentials were recorded from the vertex of subjects who listened selectively to a series of tone pips in one ear and ignored concurrent tone pips in the other ear. The negative component of the evoked potential peaking at 80 to 110 milliseconds was substantially larger for the attended tones. This negative component indexed a stimulus set mode of selective attention toward the tone pips in one ear. A late positive component peaking at 250 to 400 milliseconds reflected the response set established to recognize infrequent, higher pitched tone pips in the attended series.*

Human listeners are able to confine their attention to a single auditory message within a noisy environment and to disregard equally intense but "irrelevant" sounds. This feat of selective attention is accomplished by unknown brain mechanisms that act both to enhance the information received from selected sound sources and to suppress irrelevant, competing sensory input.

Attempts to identify neurophysiological mechanisms that uniquely subserve selective attention by recording sensory evoked potentials from animal brains have made little progress (*1, 2*). Human subjects offer distinct advantages in that their attentional processes can be accurately controlled and evaluated in conjunction with sensory evoked potentials that are recorded from the scalp. It is well established that the major components of the human auditory evoked potential—a negative component (N_1) peaking at 80 to 110 msec after an abrupt sound and a subsequent positive component (P_2) at 160 to 200 msec—are considerably larger when the sound is made "relevant" (to be attended) than when it is made "irrelevant" (to be ignored) (*3*). Naatanen (*2*) has pointed out, however, that relevant stimuli were delivered predictably in those studies, so that the effects of stimulus "relevance" upon evoked potentials could have been caused by nonselective preparatory states (for example, arousal or alertness) differentially preceding the stimuli. In experiments where the relevant and irrelevant stimuli were presented in randomized sequences that precluded differential preparatory states (*2, 4, 5*), only minimal differences were observed in N_1 and P_2.

We now report experiments in which randomized sequences of tone pips were delivered concurrently to the two ears at such a rapid rate that subjects were forced to restrict their attention to one ear at a time in order to perform a difficult pitch discrimination. Under these circumstances the N_1 evoked by tones in the attended ear was substantially larger than that evoked by tones in the opposite ear. This constitutes the first definite evidence that changes in an evoked potential component can specifically reflect selective attention as opposed to a preparatory or reactive change of nonselective state (*6, 7*).

Subjects sat in an acoustically shielded

chamber while binaural sequences of tone pips were presented through stereo earphones. In experiment 1, a sequence of 800-hz tone pips (50 db above threshold, 50-msec duration) with interstimulus intervals randomized between 250 and 1250 msec was delivered to the left ear, while an independent series of 1500-hz tone pips of similar intensity, duration, and random intervals was presented to the right ear. These concurrent binaural sequences each consisted of 512 tone pips that had been recorded earlier on an audio tape which ran for 6 minutes. About one-tenth of the tone pips in each ear had a somewhat higher frequency than the "standard" 800- and 1500-hz tone pips: the frequencies of these "signals" were 840 hz (left ear) and 1560 hz (right ear). These signals were interposed every 3 to 20 stimuli at random throughout each sequence.

The same stimulus tape was played to the subject six times in succession with a 5-minute break after each. There were three instructional conditions as follows: A, attend to the left ear, discriminate and count the number of 840-hz signals, and report the total at the end of the run; B, read a novel and disregard all tones; C, attend to the right ear and count the number of 1560-hz tones. Hereafter we refer to condition A as "attend-left" and condition C as "attend-right." Five young adult subjects received the instructional conditions in ABCCBA order and five others in CBAABC order. The reading condition was used to reduce carry-over effects between successive attend-left and attend-right conditions.

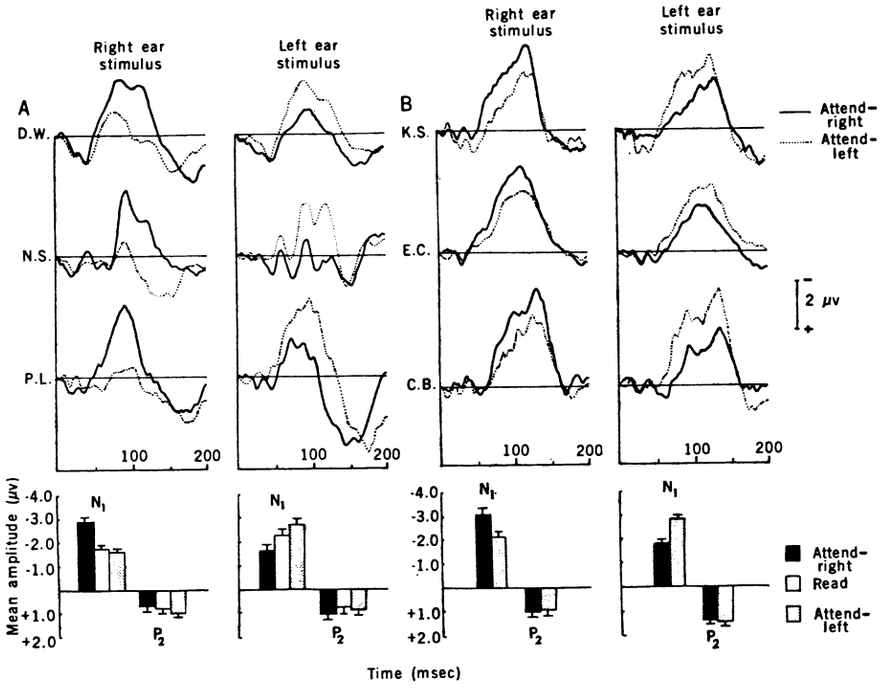

Fig. 1. (A) Vertex evoked potentials from three subjects in experiment 1. Each tracing is the averaged response to all 1024 stimuli that were presented to each ear under attend-right (solid lines) and attend-left (dotted lines) conditions. Stimulus onset is at beginning of tracing. Baselines were drawn through the mean voltage over 0 to 10 msec. Bar graphs give the mean and standard error (10 subjects) of the baseline to peak amplitudes of N_1 and P_2 evoked via each ear under all three experimental conditions. (B) Evoked potentials from three subjects in experiment 2, with bar graphs giving mean amplitudes over all ten subjects.

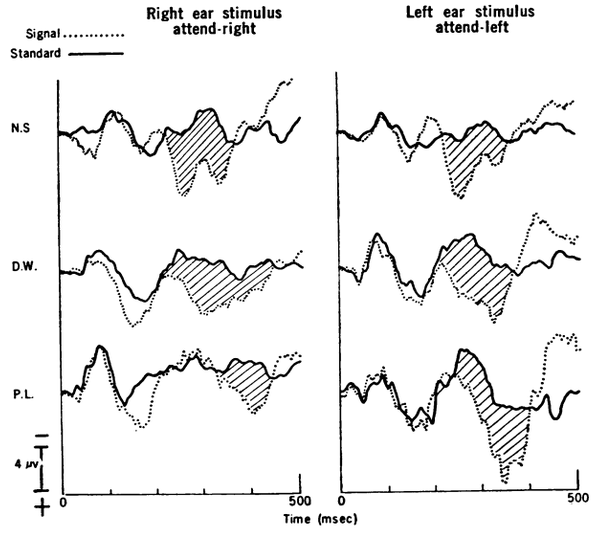

Fig. 2. The P_3 component (shaded area) evoked by signal tone pips in the attended ear. The P_3 is absent in the evoked potential to the standard tone pips (solid tracings). Each tracing is the averaged response to 90 to 110 stimuli; the standard tones were selected at random from throughout the stimulus sequence. The data are from three subjects during both experiment 1 (D.W. and P.L.) and experiment 2 (N.S.).

Evoked potentials to all stimuli were recorded from the vertex (mastoid reference) with the use of Grass amplifiers (model 6) (bandpass 1 to 70 hz) and stored on FM tape for off-line analysis on a signal averager (Fabritek 1052). Evoked vertex potentials to left and right ear stimuli were averaged separately across all 1024 tone pips (standards and signals) of an instructional condition (*8*). Electrical potentials caused by eye movements and blinks were recorded between electrodes above and below the left eye to ensure that evoked potentials were free of ocular artifacts.

In the left column of Fig. 1A, the N_1 evoked by right ear tones was considerably larger when those stimuli were attended (solid tracings) than when the left ear tones were receiving attention (dotted tracings); conversely, in the right column of Fig. 1A, larger N_1's were evoked by left ear tones during the attend-left condition (dotted tracings) than during the attend-right runs (solid tracings). These effects were observed in every subject. The amplitude of N_1 evoked by right ear tones (measured baseline to peak) was between 20 and 75 percent smaller during the attend-left as compared with the attend-right condition [mean difference = 43.5 percent; t (9) = 7.88; $P < 10^{-4}$ (two-tailed)]; conversely, the N_1 evoked by the concurrent left ear sequence was between 22 and 78 percent smaller under attend-right conditions than under attend-left [mean = 38.9 percent; t (9) = 7.28; $P < 10^{-4}$]. Thus, when attention was switched from one ear to the other, the reciprocal effects of selective attention—suppression of N_1 evoked by tones in the unattended ear and enhancement of N_1 evoked in the attended ear—were approximately symmetrical.

These manipulations produced a clear dissociation between N_1, which was an index of the direction of atten-

tion, and P_2, which was not significantly altered in either ear (Fig. 1). The effects of attention upon N_1 could not have been caused by any sustained change of nonselective state. It is conceivable, however, that very rapid fluctuations of some nonselective preparatory state might have become partially time locked to the schedule of tones in the attended ear. If such hypothetical changes of state increased all evoked potentials nonselectively, those of the attended ear would be preferentially enhanced because its stimulus schedule would be more closely coupled to the cycles of preparatory state.

To rule out these effects a second experiment was carried out in which tone pips were delivered to right and left ears according to a single sequence rather than two independent overlapping sequences as in experiment 1. Within this sequence the time intervals between successive tones were randomized between 100 and 800 msec, and each tone was delivered either to the right (800 hz) or left (1500 hz) ear with equal probability. Experiment 2 was otherwise identical to experiment 1 except for omission of the reading condition. Of the ten subjects used in experiment 2, eight participated in the previous experiment.

The results of experiment 2 paralleled those of experiment 1 (Fig. 1B). The amplitude of N_1 evoked by right ear tones was between 10 and 68 percent smaller under the attend-left condition than under the attend-right condition [mean = 30.1 percent; t (9) = 5.05; $P < 10^{-3}$]; conversely, N_1 evoked by left ear tones was 15 to 69 percent smaller when attention was shifted from the left to the right ear [mean = 34.0 percent; t (9) = 7.31; $P < 10^{-4}$]. These reciprocal effects of selective attention were on the average less than in the first experiment. Most subjects reported greater difficulty in keeping their attention on one ear when the binaural stimulus schedule was sequential, and this difficulty could explain the reduced effect. Therefore, we obtained no evidence for the thesis that cycles of nonselective alertness can exert a differential effect upon N_1 in the two ears over and above the dominant factor of selective attention.

The vertex potentials evoked by the occasional higher pitched signals in the attended ear were examined separately on a 500-msec time base. A late positive component peaking at 250 to 400 msec, P_3 (Fig. 2, shaded area), was elicited only after the signal tones and not by the standard tones (*9*).

Three features were incorporated into the present experiments which together distinguish them from earlier studies (*4, 5*) which did not reveal any substantial effect of selective attention upon N_1. First, the relevant and irrelevant stimuli differed from one another both in spatial localization and pitch attributes. This made them easily distinguishable. Second, the stimuli were delivered at such a high rate that it was impossible to discriminate stimuli in one ear and fully appreciate the stimuli to the other ear at the same time (*10*). Finally, the frequency discrimination tasks were difficult. Subjects reported hearing at most only a few of the signals in the unattended ear (*11*).

The early latency of the attention effects upon N_1 (evident at 60 to 70 msec in most subjects) suggests that the underlying attentional process is a tonically maintained set favoring one ear over the other rather than an active discrimination and recognition of each individual stimulus. Furthermore, if N_1 was enhanced after the differential recognition of relevant stimuli or a subsequent "reactive change of state" (*6*), an equivalent or larger N_1 should have occurred in the previous experiments (*4, 5*) having slower rates of stimulus presentation. The P_3, on the other hand, does seem to be elicited only upon the recognition of selected signals which require a special cognitive or motor response (*12*).

Our results suggest that N_1 and P_3 are signs of fundamentally different selective attention processes, corresponding closely to the "stimulus set" and "response set" modes of attention, respectively, described by Broadbent (*13*) and others (*14*). A stimulus set preferentially admits all sensory input to an attended channel (stimuli having in common a simple sensory attribute such as pitch, position in space, receptor surface, or the like) for further perceptual analysis, while blocking or attenuating inputs arriving over irrelevant channels (for example, the unattended ear) at an early stage of processing. Response set is a subsequent processing stage in which sensory information as compared against memorized "templates" or "models" (*7*) for selected stimuli which are not distinguishable simply by virtue of belonging to a particular sensory input channel; a response set acts to facilitate the recognition of these specific task-relevant signals.

These two hierarchical modes of attention generally operate together. At a cocktail party, for example, it is necessary to establish a stimulus set in favor of the location and pitch characteristics of a speaker's voice, and a succession of response sets to recognize the specific contents of his speech. In the present experiment we propose that the amplitude of N_1 indexes the stimulus set which selectively excludes sensory input to the unattended ear from further processing. The P_3, on the other hand, reflects the selective recognition of the higher pitched tones in the attended channel by a response set mechanism which is coupled with an appropriate cognitive response (counting) (*16*).

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6. Stimulus relevance has been shown to influence components evoked later than 175 msec in numerous experiments which controlled for possible anticipatory arousal effects. For overview see: Wilkinson and Lee (*5*) and Squires *et al.* (*7*). While such changes in long latency components (most evident in a positive wave, P_3, peaking at 250 to 400 msec) are clearly dependent upon a stimulus recognition process, it is possible that these late waves are signs of a nonselective reactive change of state which *follows* recognition of the signals [L. Karlin, *Psychol. Bull.* **73**, 122 (1969)]. Recently, J. Ford, W. Roth, S. Dirks, B. Kopell [*Science* **181**, 465 (1973)] reported a dissociation between the N_2 (latency 190 to 270 msec) and P_3 (270 to 500 msec) components during an auditory and visual selective attention task. N_2 was equally enhanced for all stimuli (target and nontarget) within the attended modality, while P_3 was largest following the targets. Whether such late changes reflect selective gating of inputs or nonselective aftereffects of stimulus discrimination and recognition is still an open question.
7. K. Squires, S. Hillyard, P. Lindsay, *Percept. Psychophys.* **13**, 25 (1973).
8. As a precaution, evoked potentials were also averaged across the standard stimuli in each ear, excluding the higher-pitched signals. These averages showed similar selective attention effects upon N_1 as did the averages across all stimuli. This ensures that a long-term nonspecific arousal process, rising to a maximum prior to a signal and falling thereafter, did not differentially bias the evoked potentials in the attended ear.

9. In all subjects the largest P_3 waves were evoked after the signals in the attended ear. In several subjects a smaller P_3 was sometimes evident following the signals in the unattended ear, indicating that information from the unattended ear was occasionally being examined. No. P_3 was discernible after the standard tones in either ear. As Fig. 2 indicates, the difference between the N_1 evoked by standard as compared to signal tones was not substantial.
10. The mean interstimulus interval (for both ears together) was 375 msec in experiment 1 and 450 msec in experiment 2. Wilkinson and Lee (*5*) also delivered stimuli (one of three tone frequencies) at a rapid rate (mean interval = 673 msec) with the aim of forcing subjects to ignore irrelevant tones. They found that counting a stimulus enhanced the N_1-P_2 component by about 10 percent ($P < .05$). The authors attribute this effect to augmenting of P_2 by a positive d-c baseline shift rather than to selective attention. No independent effect upon N_1 was reported.
11. The overall percentages of the signal tones detected had the following medians (M) and interquartile ranges (R). Experiment 1, left ear (M, 90; R, 84 to 96); and right ear (M, 81; R, 70 to 92). Experiment 2, left ear (M, 88; R, 82 to 94); and right ear (M, 94; R, 90 to 98).
12. The P_3 wave (often preceded by a negative wave at 200 msec) is elicited upon the detection of many types of auditory and visual signals (*7*). A study by R. Eason, M. Harter, and C. White [*Physiol. Behav.* **4**, 283 (1969)] is a visual analog of our experiment, with stimuli being presented to the two halves of the visual field rather than to the two ears. Stimuli in the attended field evoked large waves of long latency (beyond 150 msec) which may reflect post-recognition processes (which include P_3) instead of a tonic set favoring the attended field.
13. D. E. Broadbent, in *Attention: Contemporary Theory and Analysis*, D. I. Mostofsky, Ed. (Appleton-Century-Crofts, New York, 1970), p. 51.
14. The stimulus set and response set distinction has been posed in various terms by different theorists, for example: attention and abstraction [D. E. Berlyne, in *Attention: Contemporary Theory and Analysis*, D. I. Mostofsky, Ed. (Appleton-Century-Crofts, New York, 1970), p. 25]; input selection and target selection [A. M. Treisman, *Psychol. Rev.* **76**, 282 (1969)]; filter and template [F. G. Worden and R. Galambos, *Neurosci. Res. Program Bull.* **10**, 1 (1972)].
15. In Broadbent's formulation (*13*), a response set alters the decision criterion for recognition of the selected target. The proposed relation between P_3 and response set is therefore supported by reports that P_3 amplitude is closely correlated with decision criterion during threshold detection tasks [D. Paul and S. Sutton, *Science* **177**, 362 (1972); K. C. Squires, S. A. Hillyard, P. Lindsay, *Percept. Psychophys.*, in press], and with signal likelihood (*7*). At present it is difficult to determine whether P_3 is a sign of the actual perceptual recognition process, the subsequent response activation, or of a concomitant nonspecific arousal or motivational event.
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Axonal Transport—Simple Diffusion?

Fischer and Schmatolla (*1*) proposed the existence of an axonal transport process which is resistant to colchicine. Their autoradiographic data and controls demonstrated the arrival of a small ion, via the axon, at the first synapse in the visual system within a half-hour of injection in the eye. I suggest that the process operating in their experiments is simply diffusion.

If one tentatively accepts the experimental situation as one of diffusional movement of putrescine away from the ganglion cell, where its concentration is held approximately constant by a large pool in the vitreous humor, then the diffusion equation takes the form (*2*)

$$C_x/C_0 = 1 - \text{erf}\, x/2\ (Dt)^{1/2}$$

where erf is the error function. We can substitute the experimental values for the eye-brain separation, $x = 0.03$ cm, and the shortest observed arrival time, $t = 2 \times 10^3$ seconds, and calculate the diffusion constant, D, necessary to account for the appearance of a specified fraction, C_x/C_0, of the original concentration at a point down the nerve.

If one could detect 1 percent, then a substance whose diffusion constant was as low as 3×10^{-8} cm^2 sec^{-1} could be detected. Although it is difficult to determine precisely from the autoradiograph in (*1*), there appear to be no more than one-tenth as many grains over the brain as over the retina. However, even if a concentration ratio of ½ was necessary for detection, a diffusion constant of 5×10^{-7} would suffice.

Intracellular diffusion constants of small organic and metal ions comparable in molecular weight to putrescine have been measured in both frog nerve (*3*) and muscle fibers (*4*). Since the values obtained were 100 to 500 times that needed to account for the observed movement of putrescine, it is unnecessary to hypothesize a transport mechanism other than passive diffusion. This result illustrates that diffusion will likely prevent accurate measurement of axonal transport of rapidly diffusing species over small distances on a time scale of hours.

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3. E. Koppenhoefer and W. Vogel, *Pfluegers Arch. Gesamte Physiol. Menschen Tiere* **313**, 361 (1969).
4. M. J. Kushmerick and R. J. Podolsky, *Science* **166**, 1297 (1969).

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Magid's comment conveys the impression that we have postulated a new mechanism of intraaxonal transport. In our report we described the transport of putrescine within the optic nerve, but did not speculate on the mechanism. Diffusion itself is also a transport phenomenon. Whether the described putrescine transport occurs by diffusion or any other transport mechanism cannot be concluded from our results.

Using our published data Magid estimates a diffusion constant for putrescine within the axons and compares this constant with intracellular diffusion constants of small organic and metal ions comparable in molecular weight to putrescine. In principle this method is legitimate if one compares the diffusion constant of putrescine to the diffusion constants of other putrescine-like ions. For example, Ca^{2+} is one of the ions which has putrescine-like physiological and biochemical properties. Unfortunately, the diffusion coefficient for Ca^{2+} in nerves is not known, but it is known in muscle cells (*1*). In the case of muscle the diffusion coefficient is about 100 times smaller than in pure aqueous solution. There are good reasons to assume that chemical interactions of putrescine ions with the components of a nerve cell may further reduce putrescine mobility.

Numerous experiments involving axonal transport of protein with an incorporated labeled amino acid give evidence against simple diffusion as a transport mechanism. If protein synthesis in the perikaryon is inhibited by cycloheximide or puromycin in the presence of an unphysiologically high concentration of injected labeled amino acid, the transport of this labeled free amino acid is not seen. According to Magid's hypothesis one should see diffusion of these amino acids at a speed comparable to that of putrescine. Furthermore, in experiments with colchicine in the presence of excess amounts of labeled amino acids, transport of these amino acids is not seen. Should one suppose that simple diffusion can be stopped by colchicine?

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