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THE OHIO STATE UNIVERSITY, PH.D., 1979
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THE EMERGENCE OF BEHAVIOR FROM INTEGRATED PATTERNS OF
CENTRAL AND AUTONOMIC NERVOUS SYSTEM ACTIVITY

DISSERTATION

Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate
School of The Ohio State University

By
Barbara Berger Walker, B.A., M.A.

* * * * *

The Ohio State University
1979

Reading Committee:
Curt A. Sandman
J. Dennis Nolan
David Hothersall

Approved By

[Signature]
Adviser
Department of Psychology
I would like to express my deepest gratitude to my advisor, Curt Sandman, for his careful guidance through an unlimited number of enchanted forests.

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VITA

June 19, 1952 ........................................... Born - Gloversville, New York

1974 ........................................... B.A. (with Honors), Indiana University, Bloomington, Indiana

1974 - present ........................... Teaching Assistant, Department of Psychology, Ohio State University

1975 ........................................... State of Ohio Summer Traineeship, Children's Mental Health Center, Columbus, Ohio

1976 ........................................... M.A., Ohio State University, Columbus, Ohio

1976 ........................................... State of Ohio Summer Traineeship, Columbus Area Community Mental Health Center, Columbus, Ohio

1977 ........................................... Consultant to Intermediate Care Unit at Columbus Area Community Mental Health Center, Columbus, Ohio

1977, 1978 ................................... State of Ohio Summer Traineeship, North Central Community Mental Health Center, Columbus, Ohio


PRESENTATIONS


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PUBLICATIONS


Walker, B.B., Kaemmerer, W.F. & Marks, P.A. Emotionally disturbed adolescents with somatic complaints. (Submitted)
Sandman, C.A., Walker, B.B., & Lawton, C.A. An analog of MSH/ACTH 4-9 enhances interpersonal and environmental awareness in mentally retarded adults. (Submitted)


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INTRODUCTION

Our basic conceptions of the role of the autonomic nervous system historically from Walter B. Cannon's formulation of the "fight or flight" reaction. This reaction, a massive sympathetic nervous system discharge, allegedly occurs to prepare an organism for mobilization and vigorous muscle activity in addition to protecting it against the possible consequences. This pattern of autonomic responses gradually became linked to psychological notions of "arousal" and "activation," and much evidence has accumulated to support a unidimensional continuum of "arousal" with autonomic responses serving as the measure.

The vast majority of evidence seems to comply with Cannon's formulation, but Lacey (1967) has pointed out that this compliance is revealing only in an "actuarial" sense. In other words, although they often occur simultaneously, autonomic "arousal" and behavioral "arousal" are not the same. Each is fraught with complexities, and it is incorrect to assume that they are necessarily indices of each other. In support of this idea, Lacey (1967) has presented evidence for the dissociation of autonomic and responses all thought to be an index of "arousal." Perhaps more importantly, however, Lacey has drawn attention to neurophysiological evidence demonstrating that the autonomic nervous system is not simply an effector process; there are afferent fibers which complete visceral feedback systems with the central
nervous system, and in the case of the cardiovascular system, exert inhibitory rather than excitatory effects on higher levels of the nervous system. This neurophysiological evidence is presented in the following section.

Neurophysiological Evidence Concerning Cardiovascular Influences on the Central Nervous System

Physiologists have studied homeostatic functions of the cardiovascular afferent fibers for years, and the existence of pressure-sensitive receptors (baroreceptors) in the carotid sinus and aortic arch has been well established. The baroreceptors increase their firing rates when blood pressure increases and decreases their rates of discharge when blood pressure decreases. Nerves from the carotid sinus and aortic arch join the vagus and the glossopharyngeal nerves which terminate in the lower brain stem and assist in providing homeostatic control of blood pressure to ensure survival of the organism.

Quite interestingly it appears that baroreceptors have functions in addition to these classified physiologically as homeostatic. The evidence dates back to 1929 when Tournade and Malmejac found that stimulating the carotid sinus nerve led to diminished muscle tone in anesthetized animals. Shortly thereafter, Koch (1931) increased the pressure in the carotid sinus of a dog and found that it led to decreased motor activity and even prolonged sleep. These two reports were among the first to suggest that baroreceptor activity influences higher levels of the nervous system than those needed to maintain homeostasis and that these influences are inhibitory rather than
excitatory.

The best evidence that input from the baroreceptors inhibits rather than excites cortical activity was presented approximately 20 years ago when Bonvallet, Dell and Hiebel (1954) found that electrocortical activity shifted from low-voltage-fast to high-voltage-slow activity when the carotid sinus was distended. In addition, Bonvallet, Dell and Hugelin (1954) demonstrated that evoked monosynaptic reflexes could be inhibited by increasing pressure in the carotid sinus; the inhibition was reversed when they cut the vagus and the glossopharyngeal nerves. This demonstrated that the shifts in cortical activity observed by Bonvallet et al. (1954) were not merely a result of homeostatic mechanisms working to reduce blood pressure.

More recent experiments demonstrate inhibitory effects in areas of the brain that are quite remote from areas that have been associated with cardiovascular control. Coleridge, Coleridge and Rosenthal (1976), for example, found that distension of the carotid sinus causes prolonged depression of activity of pyramidal tract cells in the motor cortex. This depression ranged from a 15% reduction in firing to complete cessation of activity and lasted approximately 85 seconds after the distension ceased. Gahery and Vigier (1974) showed that stimulation of baroreceptor afferents also depresses the responses of single cells in the nucleus cuneatus to skin stimulation. These data emphasize that baroreceptors play an inhibitory role in sensory and motor functions as well as in the control of blood pressure.

The question arises concerning the mechanism of this inhibition. One possibility is the ascending bulbar inhibitory mechanism described
by Bonvallet and Bloch (1961) and Bonvallet and Allen (1963). They have localized this mechanism in the nucleus tractus solitarius, which is independent of homeostatic functions and replete with afferent cardiovascular fibers. That the cardiovascular system has some control of activity in this area is evidenced by the fact that cells firing with a cardiac rhythm have been recorded in this area (Humphrey, 1967; Smith & Pearce, 1961), and when the glossopharyngeal and the vagus nerves are cut, cortical activation is prolonged (Bonvallet & Allen, 1963). This bulbar system appears to be triggered by the reticular activating system and has been found to inhibit cortical, autonomic and somatomuscular activity (Bonvallet & Allen, 1963). Coagulations in this area prolong the effects of stimuli rather than change them. Lacey (1967) has suggested that the function of this area seems to be to "control the duration of an episode of stimulus-produced activating processes in the brain" (p. 27).

The neurophysiological evidence alluded to by the Laceys suggests that blood pressure increases encoded by baroreceptors are transmitted via the vagus and the glossopharyngeal nerves to the area of the brain stem maintaining homeostasis and to an area which serves to inhibit cortical, autonomic (except cardiovascular) and muscular activity. It is unclear whether this inhibition may be attributed specifically to the ascending bulbar inhibitory area described by Bonvallet and her colleagues, but it is clear that the role of the cardiovascular afferents in this inhibitory process is separable and independent from their role in maintaining physiological homeostasis. According to this model, increases in blood pressure are seen as part of an
inhibitory or restraining process rather than an activating process. Conversely, decreases in blood pressure are seen as a release of this inhibition implying a lowering of sensory thresholds and a prolongation of stimulus impact.

The complexities and problems associated with this model have not gone unrecognized by the Laceys (see Lacey, 1967). One problem arises as a result of the fact that the carotid sinus is not purely passive. It has its own properties, and Peterson (1962) has shown that the stiffness of the carotid sinus wall, one determinant of baroreceptor sensitivity, is affected by acetylcholine and norepinephrine. It seems clear that other nervous system activity may alter the stiffness of the wall and the sensitivity of the baroreceptors. The inhibition thought to be determined by baroreceptor activity may in reality be determined by other nervous system activity affecting the wall of the carotid sinus.

In view of this, it is not surprising that inhibitory effects do not occur every time blood pressure increases. It is clear that the central nervous system modifies the cardiovascular-central nervous system relationship partly as a result of other input. Exercise, for example, will not necessarily lead to inhibitory effects on the organism. The inhibition is subject to modification by higher levels of the central nervous system not only from the level of the wall of the carotid sinus itself to the area of the brain it ultimately reaches, but also from the area of the brain back to the effector processes where inhibition is observed.
Another complication is the fact that there are many baroreceptors throughout the body in addition to those in the aortic arch and carotid sinus. It would be naive to assert that only those in the aortic arch and carotid sinus bear any relationship to the central nervous system and behavior. Undoubtedly, there are complex interactions at many levels of the nervous system among various baroreceptor systems that are scattered throughout the body. Virtually nothing is known at this point regarding these possible interactions.

The temporal sequence of baroreceptor discharge poses another problem. Frequency of baroreceptor firing may be slightly out of phase with changes in blood pressure. Furthermore, little is known concerning the interaction between tonic levels of blood pressure and phasic changes in blood pressure even at the level of the baroreceptors.

Finally, the role cerebral blood flow plays in this inhibitory process is unclear. When carotid baroreceptors are stimulated, there is a decrease in arterial blood pressure which may lead to a significant fall in cerebral blood flow. Diminished cerebral blood flow causes a decrease in oxygen available to the tissues which might account for neuronal inhibition. While the widely accepted view is that cerebral blood flow is autoregulatory and not subject to any significant neurogenic control (see Purves, 1972 for a review), there are data to indicate that cerebral vasoconstriction occurs when systemic blood pressure is raised and that this vasoconstriction is related specifically to baroreceptor activity (Ponte & Purves, 1974). It is possible, therefore, that increases in baroreceptor firing lead to cerebral vasoconstriction which in turn leads to neuronal inhibition.
The situation is complicated, however, since Ingvar and his colleagues (1971; 1972) have emphasized that cerebral blood flow is regulated by the metabolic activity of neuronal tissue. Decreases in neuronal activity lead to a decrease in carbon dioxide output and an increase in extracellular pH giving rise to cerebral vasoconstriction. Thus, while it is certain that neuronal activity and cerebral blood flow are closely coupled, the precise nature of the relationship is unknown.

The complexity of the interactions in this system is enormous. For this reason, the Laceys have made it clear that no simple formulas can be proposed which will apply in each situation. The effects of the cardiovascular system on the central nervous system are at times, however, reflected in the behavior of the organism in spite of the complexities. The following section presents the psychophysiological evidence that in certain specific circumstances, pressor responses are restraining or inhibitory whereas depressor responses appear to release this restraint and prolong stimulus impact.

Psychophysiological Evidence Concerning Cardiovascular Influences on the Central Nervous System and Behavior

Lacey, Kagen, Lacey and Moss (1963) found that only heart rate and blood pressure differentiated tasks requiring attention to input (i.e., detecting flashes) from those in which attention to the environment would be detrimental to performance of the tasks (i.e., mental arithmetic). The authors suggested that "mental concentration" is accompanied by heart-rate acceleration and attention to the environment is accompanied by heart-rate deceleration.
Results of experiments on reaction time provided some initial support for this speculation. Heart rate characteristically decelerates three or four beats before the imperative stimulus in a reaction time experiment, with the lowest point frequently occurring precisely at the onset of the stimulus. If the speculations of the Laceys are correct, one would expect the magnitude of this deceleration to be positively correlated with reaction time. Several authors have found this to be true (Coquery & Lacey, 1966; Lacey & Lacey, 1974; Obrist, Webb, & Sutterer, 1969; Lacey & Lacey, 1970; Duncan-Johnson & Coles, 1974); the greater the cardiac deceleration, the faster the reaction time.

The relationship between heart rate and behavior has since been demonstrated in a variety of paradigms such as complex problem solving (Kaiser & Sandman, 1975), visual search (Coles, 1972), auditory threshold (Saxon & Dahle, 1971), and during stressful stimuli (Hare, 1973; Sandman, 1975; Walker & Sandman, 1977). Moreover, instrumental relationships between heart rate and both visual perception and cognitive processing have been demonstrated. Tachistoscopic stimuli presented during operantly conditioned cardiac deceleration are perceived more accurately than stimuli presented during conditioned acceleration (McCanne & Sandman, 1974). In another study, operantly conditioned increases in heart rate led to the generation of more counterarguments to persuasive message (indicating facilitated cognitive processing) than conditioned decreases in heart rate (Cacioppo, Sandman, & Walker, 1978).
As stated earlier, baroreceptors encode changes in blood pressure. In general, increases and decreases in heart rate coincide with increases and decreases in blood pressure and baroreceptor firing. In addition to blood pressure changes that are related to heart rate, however, there are blood pressure changes that occur within each cardiac cycle and baroreceptors respond to these changes as well. With each ventricular contraction (occurring at the R wave of the EKG), blood is forced through the carotid sinus and at the peak of that pulse pressure wave (near the T wave of the EKG), the baroreceptors are maximally active. Baroreceptors are minimally active when the carotid pulse pressure wave is at its lowest point (near the P wave of the EKG). The pressure at the highest and lowest points in the pulse pressure wave are referred to as systolic and diastolic pressure and mean blood pressure is the average of these two readings taken over a period of several heart beats.

Since the relationship between heart rate and behavior has been attributed in part to baroreceptor activity, the fact that baroreceptors fire differentially within each cardiac cycle suggests that there may be a relationship between cardiac phase and behavior. Specifically, the P wave in the EKG might be related to behavioral changes associated with low heart rate whereas the T wave might be associated with behavioral changes similar to those observed at high heart rate. Two early studies reported that reaction time varied as a function of where in the cardiac cycle the stimulus was presented (Birren, Cardon & Phillips, 1963; Callaway & Layne, 1964), but three later studies failed to show any effect of cardiac phase on behavior (Thompson & Botwinick,
1971; Elliott & Graf, 1972; Delfini & Campos, 1972). More recently, however, Saari and Pappas (1976) demonstrated a relationship between cardiac phase and reaction time, and Sandman, McCanne, Kaiser and Diamond (1977) demonstrated that visual perception was more acute when stimuli were presented early in the cardiac cycle than when they are presented late in the cardiac cycle.

These data regarding the relationship between cardiac phase and behavior are equivocal. Even in studies that have demonstrated relationships, the effects are not as robust as those observed with changes in heart rate (e.g., Sandman et al., 1977). It seems clear that baroreceptor firing depends upon complex interactions between heart rate and systolic, diastolic and mean blood pressure. The Laceys (1974), for example, have reported that the relationship between heart rate and reaction time is significantly greater when stimuli are presented during diastole than when they are presented during systole. They have suggested that electrical systole may disturb events associated with heart rate and, in addition, that cycle effects may be dependent to some extent upon heart rate.

While it appears that the relationship between heart rate and behavior is somewhat more clear at this point than is that between cardiac phase and behavior, many questions remain unanswered. The findings presented by the Laceys suggest that it is the interaction between heart-rate level and cardiac phase that is behaviorally significant. This is difficult to assess at this point however, because few studies have been undertaken to investigate the influences of heart rate, cardiac phase, and the interaction of the two using the same
paradigm. The behaviors that have been examined are limited; most investigators have studied simple reaction time or sensory thresholds. Furthermore, some investigators have used operant conditioning techniques to achieve changes in heart rate, and it is unknown how the use of this procedure may affect the intricate relationship between cardiac activity and behavior. In addition, concomitant changes in EEG have rarely been examined; this seems to be of critical importance, particularly in view of the neurophysiological evidence cited earlier.

One measure of electrocortical activity, the average evoked response (AEP), is exquisitely sensitive to changes in the attentional state of the organism (Haider, Spong & Lindsley, 1964) and therefore seems particularly well-suited for investigating relationships between cardiovascular and central nervous system activity. The following studies were designed to examine these relationships using a paradigm unconfounded by behavioral requirements. The first experiment focuses on changes in the AEP that are related to changes in normally fluctuating heart rate, the second is a study of electrocortical changes that are related to changes in carotid pulse pressure, and the third is an examination of changes in the AEP that are related to the interaction between heart rate and carotid pulse pressure.

There is a well-documented asymmetry of brain functioning with the right hemisphere relating to intuitive, spatial abilities and the left relating to logical, rational abilities (see Sperry, 1973 for a review). The fact that the two hemispheres respond differently to many types of stimulation provides a rationale for separate analyses of evoked responses recorded from the right and left cerebral hemispheres.
If the two hemispheres are related differently to cardiovascular activity, then it is conceivable that the cardiovascular system selectively influences cortical activity. While the different behavioral effects associated with cardiovascular changes are not identical to those proposed for the two hemispheres, there are some similarities. For instance, transient tachycardia may be related to activity of the left hemisphere since both have been related to logical thoughts and cognitive elaboration. Similarly, bradycardia may be related to the right hemisphere since both have been associated with attentional processes. The possibility that the cardiovascular system influences behavior by differentially stimulating the two hemispheres has not been previously suggested and therefore was of considerable interest in the following experiments.
EXPERIMENT I
Influences of Heart Rate on the Visual Evoked Response

Introduction

As discussed earlier, neurophysiological research with animals indicates that changes in the cardiovascular system are related to changes in electroencephalographic activity, and several studies with human subjects indicate that cardiovascular changes are reflected in behavior. In view of this, it is surprising that so few studies with human subjects have focused on the relationship between cardiovascular and central nervous system activity. It appears as if investigators concerned with heart rate and behavior have been relatively unconcerned with the concomitant electrocortical activity and those concerned with electrocortical changes have been relatively unconcerned with heart rate.

The purpose of the present experiment was to examine the electrocortical changes that are associated with changes in heart rate in healthy human subjects. Since the amplitudes of the P1 and P2 waves of the AEP have been associated with enhanced attention (Spehlmann, 1965; Callaway, 1975), it was hypothesized that these waves would be enhanced during low heart rate. On the other hand, the amplitude of the P3 wave has been related to cognitive activity (Sutton, 1969; Donchin & Cohen, 1966; Beck, 1975) and it was speculated that this
component might be enhanced during high heart rate.

Method

Subjects

Men who wanted to participate in the study as part of a requirement for Introductory Psychology classes at Ohio State University were screened and 16 who met the following criteria were selected to participate: 20/20 corrected vision, right-handed, between the ages of 18-25, absence of drug usage, variable heart rates, no evidence of high blood pressure or any cardiovascular pathology, and absence of sleep difficulties.

Procedure

The subjects reclined in a comfortable chair while transducers were attached for recording heart rate, cephalic blood flow, respiration, EEG and eye movements. Care was taken to insure that each subject was in a position that did not entail continuous postural tension. Each subject wore headphones with masking noise to eliminate all extraneous auditory stimuli. A dot was positioned for each subject individually so that it was directly in front of him, and each subject was instructed to fixate on the dot at all times. They were also instructed to relax, breathe regularly and to keep their eyes open at all times. There were three rest periods given during each session; these were signified by turning the masking noise off for a few minutes. After a few minutes of rest, midrange heart rate was calculated, and in accordance with Sandman et al. (1977), criteria for low and high heart rate were defined as the slowest and the fastest
decile of the heart beats. One-minute baseline heart rates were recalculated and criteria were reset approximately every five minutes to correct for changing baselines.

**Apparatus**

The subjects were tested in a sound-attenuating and electrically shielded room. The recording, programming and stimulus presentation equipment were housed in an adjacent room. Physiological recordings were obtained with a Grass Model 7B polygraph equipped with the appropriate preamplifiers and driver amplifiers. In addition to being recorded on the polygraph, both channels of EEG (right and left hemispheres) were recorded on a four channel Sony FM tape recorder to enable computer analyses of these data. The voltage changes associated with heart rate (obtained from the output of the tachograph) were detected with a BRS digibit logic system (Model 310 Schmidt triggers and Model 201 level detectors) which compared the signal to the preset criterion. When criterion for high or low heart rate was met or exceeded, a 20-msec flash was projected on the screen by a Kodak projector tachistoscope. Flashes occurred at midrange heart rate when heart rate was below the criterion set for high heart rate and above the one set for low heart rate. The logic units were programmed so that a minimum of four seconds elapsed between flashes. Each stimulus was marked on the tape and coded using a varying voltage for high, midrange, and low heart rates. Each subject received 150 flashes: 50 at high heart rate, 50 at midrange heart rate and 50 at low heart rate. These were delivered in blocks of 10 so that one third of the flashes at each level occurred at the beginning of the session, one third in
the middle of the session and one third at the end of the session.¹

**EEG.** Sites designated by the international 10-20 system (Jasper, 1958) as O₁ and O₂ and both mastoids were rubbed briskly with acetone to reduce resistance. Ag-AgCl electrodes filled with Grass EEG Creme were then affixed to the scalp with collodion and linked from O₁ to mastoid and O₂ to mastoid to enable unipolar recordings from the right and left occipital cortex. Pairs of electrodes showing more than 10,000 ohms of resistance were replaced. The signal was amplified by a Grass AC preamplifier with the low frequency filter set at 1 Hz (which corresponds to a time constant of .1 second) and the high frequency filter set at 35 Hz (Goff, 1974).

**Heart Rate.** Grass cup electrodes filled with EKG Sol were attached to the area of the lower left rib and the right collar bone of each subject after these areas were swabbed with acetone. The signal was amplified by a Grass AC preamplifier and processed by a cardio-tachometer to provide beat-by-beat heart-rate recordings.

**Respiration.** The respirometer consisted of a thin-walled opaque neoprene tubing 5.1 cm in length and 3.5 mm in diameter with an optical sensor and emitter mounted at each end. The mounting was roughly spherical with a diameter such that the tubing, when stretched across the chest, was drawn taut in a straight line between mounts. Attached to each mount was a cloth band 1.95 cm in width and of sufficient length to encompass different chest sizes. Velcro fasteners on each end held the respirometer in place. Current output of the phototransistor was approximately linear with chest expansion. The varying voltage was amplified by a Grass AC preamplifier.
Cephalic Blood Flow. A plethysmograph containing a light-emitting diode (LED) and a narrow band emitter of infrared radiation with a wavelength of .74 micrometers was placed over the supraorbital notch, temporal to the nasium. The emitter of the plethysmograph was placed in the same plane as a photodarlington resistor of matched sensitivity. The two devices were mounted on a small glass epoxy printed circuit. The signal was amplified by a Grass AC preamplifier and provided a relative measure of blood flow in the supraorbital artery, a branch of the ophthalmic artery (Wallace & Wallace, 1968).

Eye Movements. Ag-AgCl electrodes were placed next to and below the left eye about 2 cm from the orbital cavity using Grass EKG Sol. The signal was amplified by a Grass AC preamplifier. The purpose of this measure was to enable detection of all trials involving eye movements or eye blinks.

Data Reduction

Averaged Evoked Potentials. Electrocortical activity associated with the 50 flashes at low heart rate, the 50 flashes at midrange heart rate and the 50 flashes at high heart rate was converted from analog to digital at a sampling rate of 100 Hz for a period of 500 msec following the flash. These data were then averaged and graphed using a Nova 3/12 computer system yielding three averaged evoked potentials (AEPs) for each hemisphere for each subject.

Three measurements were taken for each of the six AEPs obtained for each subject: peak delay, wave component amplitude, and an overall amplitude measure (Dustman et al., 1976). Peak delay refers to the
measurement (in msec) from the onset of the stimulus to the positive peak occurring approximately 100 msec following the flash (P1), one occurring approximately 200 msec following the flash (P2), and one approximately 300 msec following the flash (P3). Wave component amplitude refers to the voltage difference between two consecutive peaks of opposite polarity (measured in microvolts). This measure was taken for P1, P2 and P3. Overall amplitude refers to the total voltage change occurring from the onset of the flash to 500 msec after the flash. This was obtained by subtracting the voltage associated with the lowest negative peak from the voltage associated with the highest positive peak.

Identification of the prominent peaks in the AEP is sometimes difficult due to large interindividual variability in AEP waveforms. Therefore, two independent judges chose the peaks in each AEP. The mean of the interrater reliability coefficients computed for each subject was .98, indicating that the three peaks were quite clearly represented in all but a few of the waveforms obtained.

Heart Rate. The rate of five heart beats was recorded for each flash: two beats prior to the stimulus, the beat during which the stimulus occurred, and two beats following the stimulus.

Cephalic Blood Flow. The amplitude of the cephalic pulse immediately prior to the stimulus and the one immediately following the stimulus were measured in millimeters and converted to millivolts.

Respiration. Frequency and depth of respiration were monitored but not subjected to analysis. Flashes associated with dramatic changes in respiration were repeated. Few such occurrences were noted.
Eye Movements. Trials associated with eye movements and eye blinks were repeated. No further analyses of eye movements were conducted.

Results

Heart Rate. To test whether the flashes of light actually occurred at different heart rates, a 3 (heart-rate levels) x 50 (trials) x 5 (heart beats) analysis of variance with repeated measures of all the factors was performed. This analysis revealed a highly significant interaction between heart rate levels and heart beats, F(8,120) = 49.96; p < .001, which is shown in Figure 1. As illustrated in the figure, the mean heart rate for the beat that triggered the stimulus at low heart rate was approximately 14 beats per minute slower than the beat that triggered the stimulus at high heart rate. The analysis also revealed a significant main effect for trials, F(49,735) = 4.95; p < .001, indicating that heart rate significantly decreased from the beginning to the end of the session.

Heart Rate and the AEP. To test whether changes in heart rate were associated with changes in the evoked potentials recorded from the two hemispheres, the AEPs associated with high, midrange and low heart rates were averaged for all subjects for both hemispheres separately. This yielded three AEPs associated with the right hemisphere and three associated with the left hemisphere which are illustrated in Figure 2. Donchin (1969) demonstrated that stepwise discriminant function analysis (Rao, 1965) is one of the most powerful multivariate statistical procedures for determining the AEP components.
Heart rate (beats per minute)

$\begin{array}{c}
20 \\
74 \\
70 \\
68 \\
66 \\
64 \\
62 \\
60
\end{array}$

- **High heart rate**
- **Midrange heart rate**
- **Low heart rate**

Heart beats before, during, and after the stimulus

**Figure 1**

Heart rate two beats before the stimulus, during the stimulus, and two beats following the stimulus for each heart rate level.
Figure 2

Averaged evoked response waveforms associated with low heart rate, midrange heart rate and high heart rate. The arrows on the abscissa indicate points in the waves that were significantly differentiated by the discriminant function analysis. Upward deflections denote positivity of the occipital electrode.
that are most directly involved in differentiating various waveforms. In a stepwise discrimination analysis (Dixon, 1977; BMDP7M), each time point in the AEP is scanned, one at a time, and the one point which yields the best discrimination between the groups is selected. The program then computes canonical correlations and coefficients for the canonical variables. The first canonical variable is the linear combination of variables entered that best discriminates among the groups. The second variable is the next best linear combination orthogonal to the first. The group means and all cases are then plotted using the first two canonical variables as axes.

The evoked potentials recorded from the right and the left hemisphere were analyzed separately using this procedure. It was found that 17 points significantly differentiated the three waveforms recorded from the right hemisphere; no additional points yielded significant improvement in the discrimination. These points are indicated (with arrows) in Figure 2. The scatter plot shown in Figure 3 illustrates the clear separation of the three groups. The F matrices generated by comparing only two groups at a time revealed that the significant differences occurred primarily because the AEP associated with low heart rate was significantly different from the AEPs associated with mid-range and high heart rate. Using the discriminant function generated, 81.3% of the AEPs recorded at low and midrange heart rate were classified correctly, but only 50% of those recorded at high heart rate were classified correctly.  

Results of the stepwise discriminant analysis for the AEPs recorded from the left hemisphere were remarkably different. Several
points were statistically significant in differentiating the three waveforms (shown in Figure 2), but these differences occurred primarily because the AEP associated with midrange heart rate was significantly different from those associated with low and high heart rate. No points significantly differentiated the AEP associated with low heart rate from the one associated with high heart rate. This can be seen clearly in the scatter plot illustrated in Figure 4. Using the discriminant function generated, only 37.5% of the AEPs recorded at high heart rate and 50% of those at low heart rate could be classified correctly whereas 100% of those recorded at midrange heart rate were classified correctly.

The wave component amplitudes and peak delays that were obtained for each subject were averaged for all the subjects and the smooth curves drawn to fit the amplitudes and latencies of the peaks are illustrated in Figure 5. To examine the relationship between heart rate and wave components amplitudes, a 3 (heart-rate levels) x 2 (hemispheres) x 3 (peaks) analysis of variance with repeated measures of all the factors was performed. This analysis revealed a significant interaction between heart-rate levels, hemispheres, and peaks $F(4,60) = 5.84; p < .01$, which is illustrated in Figure 6. For the right hemisphere, P1 and P2 were largest in the AEP elicited at low heart rate whereas P3 was largest for the AEP elicited at high heart rate. Peak amplitudes associated with the left hemisphere were remarkably different from those associated with the right; the only notable similarity was that in both hemispheres the amplitude of P3 was largest for the AEP associated with high heart rate. Simple
Scatter plot of the group means (numbered) and individual cases (lettered) for the right hemisphere using the first two canonical variables as axes.
Figure 4

Scatter plot of the group means (numbered) and individual cases (lettered) for the left hemisphere using the first two canonical variables as axes.
Figure 5

Peak delays and wave component amplitudes associated with P1, P2 and P3.
Wave component amplitudes of P1, P2 and P3 associated with the right and left hemispheres.
effects tests revealed that there were no significant main effects of
heart-rate level for any of the three peaks in either hemisphere. A
3 (heart-rate levels) x 3 (peaks) analysis of variance with repeated
measures of all the factors was used (for the two hemispheres
separately) to test the relationship between heart rate and peak delays.
There was a significant interaction between levels and peaks in the
left hemisphere, F(4,60) = 3.82; p < .01, indicating that when flashes
were elicited at midrange heart rate, P1 and P2 occurred later and P3
occurred earlier than when flashes were elicited at high or low heart
rate. No significant differences were detected in the right hemisphere.

The overall amplitudes were analyzed using a 3 (heart-rate levels)
x 2 (hemispheres) analysis of variance with repeated measures of all
the factors. The results indicated that AEPs elicited by midrange
heart rate were significantly smaller than those elicited by either
high or low heart rate, F(2,20) = 4.12; p < .05, for the main effect;
p < .05 for Scheffé test. Furthermore, a significant interaction
between heart-rate levels and hemispheres emerged, F(2,30) = 3.76;
p < .02, revealing that the greatest overall amplitude in the right
hemisphere was associated with low heart rate whereas the greatest
overall amplitude in the left hemisphere was associated with high heart
rate. Simple effects tests, however, indicated that there were no
significant main effects of heart-rate level for either hemisphere.

Cephalic Blood Flow. A 3 (heart-rate levels) x 50 (trials) x 2
(periods; pre-stimulus/post-stimulus) analysis of variance with
repeated measures of all the factors was used to examine the relation­
ship between heart rate and cephalic blood flow. This analysis
Cephalic pulse amplitudes preceding and following stimuli elicited at low, midrange and high heart rate.
revealed a highly significant interaction between heart-rate levels and periods, \( F(2,30) = 11.45; \ p < .001 \), shown in Figure 7. As shown in the figure, cephalic pulse amplitude was largest following slow heart beats and smallest immediately following fast beats. This finding not only confirms findings of other studies (Ingvar, 1971; Sandman et al., 1977) but emphasizes the fact that these changes are specifically related to changes in heart rate.

**Summary of Results**

These results, taken together, indicate that spontaneous changes in heart rate are related to changes in central nervous system activity. Furthermore, it appears that changes in heart rate are reflected in the two cerebral hemispheres differently. Discriminant function analyses indicated that the AEPs recorded from the right hemisphere that were associated with low and high heart rate could be differentiated from each other but those recorded from the left hemisphere could not. The amplitudes of P1 and P2 were largest (in the right hemisphere) when stimuli were elicited by slow heart beats whereas the amplitude of P3 was largest (in both hemispheres) when flashes occurred during fast heart beats. The overall amplitudes of the AEPs associated with midrange heart rate were significantly smaller than the overall amplitudes of those related to low or high heart rate. Furthermore, the overall amplitudes in the right hemisphere were largest during low heart rate whereas those in the left hemisphere were largest during high heart rate. Heart rate was also related to changes in cephalic blood flow, suggesting that the relationship
between heart rate and the brain is not limited to changes in electro-cortical events.

Discussion

In the present study, spontaneous changes in heart rate were related to changes in both the primary and secondary components of the visual evoked response. The primary response of the AEP, which is "sensory receiving" in function (Lindsley, 1969; Beck, 1975; Regan, 1972) was entirely absent from the right hemisphere and diminished in the left when stimuli were elicited during slow heart beats (see Figure 2). This component of the AEP is believed to represent specific and direct impulses travelling from the receptor organ to the lower layers of the cortex via specific thalamic nuclei (Lindsley, 1969; Beck, 1975). In view of the fact that it remains unchanged under anesthesia, during sleep, and during changes in the psychological state of an organism (Dustman et al., 1976), the relationship between heart rate and this component is particularly surprising. Nevertheless, several possibilities could account for such a change.

One possibility is that the baroreceptors influence a very direct and specific pathway involving the retina, the lateral geniculate nucleus and the lower layers of the occipital cortex. Changes in the primary response have generally been associated with this specific pathway rather than with nonspecific pathways involving the midbrain and reticular formation (Lindsley, 1969). Reticular stimulation has been shown to influence the primary auditory evoked response in cats (Galambos, 1956), however, and this suggests that nonspecific pathways
also may be involved. Thus, it is also possible that the ascending bulbar inhibitory mechanism postulated to account for behavioral changes associated with heart rate accounts for these changes in the primary evoked response.

Another possible explanation of these results is that cells in the brain that control cardiovascular activity simultaneously influence electrocortical events. This is highly speculative, however, since although there are cells in the brain stem known to fire at a cardiac rhythm (Humphrey, 1967; Smith & Pearce, 1961), the cortical representation of this neuronal activity has not yet been elucidated. Further, if this explanation were viable, it would be expected that distinctive electrocortical activity would be coupled with cardiovascular activity. While attempts have been made to relate cardiac changes to characteristics of the EEG (Callaway & Buchsbaum, 1965; Callaway & Layne, 1964), the evidence for this relationship is sparse and equivocal.

The secondary components of the AEP were also associated with changes in heart rate. These components have been related to impulses conducted by way of a nonspecific and indirect system possibly via the reticular formation or midline thalamic nuclei (Jasper, 1960; Rose & Lindsley, 1965; 1968; Goff, Rosner, & Allison, 1962; Bergamini & Bergamasco, 1967) and are sensitive to changes in attention and levels of consciousness (Haider et al., 1964; Nääätänään, 1975; Dustman et al., 1976). In the present study, the amplitudes of P1 and P2 were largest (in the right hemisphere) when stimuli were elicited during slow heart beats, but the amplitudes of P3 were largest (in both hemispheres) when stimuli were elicited during fast heart beats.
Psychophysiological investigations have shown that positive peaks occurring approximately 100 and 200 msec after the stimulus are associated with relatively simple perceptual processing such as pattern perception (Spehlmann, 1965; Callaway, 1975), whereas the positive peak occurring approximately 300 msec after the stimulus is associated with more complex cognitive activity such as decision-making (Sutton, 1969; Donchin & Cohen, 1966; Beck, 1975). Since increases in heart rate have been related to cognitive processing (Lacey et al., 1963; Kaiser & Sandman, 1975; Walker & Sandman, 1977; Cacioppo et al., 1978) and decreases have been related to the facilitation of sensory "intake" (Lacey et al., 1963; Lacey, 1967; Sandman et al., 1977), the changes in the amplitudes of the secondary components observed in the present study are consistent with formulations derived from behavioral studies regarding both the behavioral significance of heart-rate changes and the nonspecific pathway that has been associated with the cardiovascular-behavior relationship.

In the present study, cephalic pulse amplitudes were largest when heart rate was low and smallest when heart rate was high. This finding not only confirms findings of Ingvar (1971, 1972) and others (Sandman et al., 1977), but provides compelling evidence that these cerebrovascular effects are specifically related to changes in heart rate. Evidence from behavioral studies has also suggested that changes in cerebral blood flow may be related to cardiac influences on the brain and behavior. Bonvallet and her colleagues (1961, 1963) have demonstrated that electrocortical activity slows when blood pressure is increased, and Ingvar (1971) has related this slowing of the EEG
to cerebral vasoconstriction. Interestingly, cephalic vasoconstric-
tion has also been related to the brief periods of perceptual insensi-
tivity that occur during fast heart beats (Sandman et al., 1977).
These converging lines of evidence suggest that cerebral flood flow
may play an intervening role in the relationship between cardiac
activity and behavior.

Research conducted in divergent areas is beginning to suggest
interrelationships among physiological systems associated with atten-
tional processes. For instance, changes in level of attention are con-
sistently reflected in evoked responses recorded from the right hemi-
sphere but not from the left (Dustman et al., 1976). Further, as
reviewed earlier, the Laceys (1963, 1967) have proposed that attention
is related to heart rate deceleration. In support of these indepen-
dent observations, the present study indicates that changes in heart
rate are reflected more clearly in the right hemisphere than the left.
Furthermore, the overall amplitudes of evoked responses in the right
hemisphere are enhanced during low heart rate and the amplitudes in
the left hemisphere are enhanced during high heart rate. This sug-
gests that the relationship between heart rate and various behaviors
may be a result of different types of activity occurring in the two
cerebral hemispheres.
EXPERIMENT II
Influences of Carotid Pulse Pressure on the Visual Evoked Response

Introduction
Baroreceptors respond to changes in blood pressure that occur within one cardiac cycle as well as to changes in heart rate. With each ventricular contraction, blood is pumped through the carotid artery creating a pulse pressure wave. The highest and lowest points of this wave are referred to as systolic and diastolic pressure. The baroreceptors situated in the wall of the carotid sinus are maximally active at systolic pulse pressure and relatively inactive at diastolic pressure. These relationships are shown in Figure 8 which also illustrates that systolic pressure generally coincides with the T wave of the EKG whereas diastolic pressure coincides with the P wave.

The fact that the effects of fluctuating heart rate levels are summarized within each cardiac cycle led some investigators to suggest parallel relationships between cardiac phase and behavior and heart rate and behavior. Since baroreceptors increase their firing rate during both high heart rate and systolic pressure, for example, it was speculated that performance on a reaction time task might be impaired during systolic pressure as it is during high heart rate. Similarly, baroreceptors are relatively inactive during both low heart rate and
Relationships between heart rate, EKG, carotid pulse pressure and baroreceptor activity.
diastolic pressure which suggests that reaction time might be facilitated during diastolic pressure as it is during low heart rate.

As indicated earlier, there have been several attempts to demonstrate similarities between behavioral effects of changes in heart rate and changes within a cardiac cycle. The data are equivocal. Although two early studies demonstrated relationships between cardiac phase and behavior (Birren et al., 1963; Callaway & Layne, 1964), three later ones failed to show any effects (Thompson & Botwinick, 1971; Elliott & Graf, 1972; Delfini & Campos, 1972). More recently, relationships between cardiac phase and reaction time (Saari & Pappas, 1976) and visual perception (Sandman et al., 1977) have been demonstrated, but the effects in these two studies were not nearly as robust as those that have been observed with changes in heart rate.

One reason for these equivocal results regarding the significance of cardiac phase for behavior may be that investigators have focused on the electrical events in the EKG rather than on the carotid pulse wave itself. It has been presumed that the P wave in the EKG coincides with diastolic pressure and that the T wave coincides with systolic pressure. The relationship between the carotid pulse pressure wave and the EKG, however, is not as clear as was presumed; peak systolic pressure often occurs slightly before the T wave (see Netter, 1978; Langley, 1971) and all of these relationships vary slightly with heart rate (Rushmer, 1970). Thus, presenting stimuli during the P or T wave of EKG does not ensure presentation during diastolic and systolic pressure. Along with a multitude of procedural variations among laboratories, this has made it almost impossible to determine precisely
where stimuli were actually presented with respect to the carotid pulse pressure wave.

Since baroreceptor activity is related to carotid pulse pressure and has no precise relationship to the various waves of the EKG, focusing on the carotid pulse pressure wave directly may reveal differences that have not been observed previously. Carotid pulse pressure can be monitored by placing a photoplethysmograph directly over the carotid sinus. Although Obrist and his colleagues (Obrist, Gaebeliein, Teller, Langer, Grignolo, Light & McCubbin, 1978) have studied changes in carotid blood flow as a response to stress, there are no studies as yet using carotid pulse pressure to examine cardiovascular influences on the brain or behavior.

The present study was designed to examine the relationship between carotid pulse pressure and the visual evoked response. If changes within a cardiac cycle are similar to changes in heart rate, the results of Experiment I and previous behavioral experiments suggest that the components of the AEP occurring 100 and 200 msec after the stimulus may be enhanced during diastolic pressure whereas the component 300 msec after the stimulus may be facilitated at systolic pressure. Furthermore, if changes within a cardiac cycle are similar to changes in heart rate, these relationships will be more apparent in the evoked responses recorded from the right hemisphere than from the left.
Subjects

Subjects were nine male and nine female subjects who volunteered for the experiment. All were right-handed with 20/20 corrected vision and showed no evidence of cardiovascular or central nervous system disorders.

Procedure

The procedure was similar to the one described in Experiment I except that flashes of light were elicited by systolic pressure (peaks) or diastolic pressure (valleys) as recorded from the carotid artery. Carotid pulse pressure was monitored by placing a photoplethysmograph (described in Experiment I for cephalic blood flow) directly over the carotid artery. The signal was amplified using a Grass AC preamplifier with a time constant of 0.08 and half amplitude high frequency of 15 hz. The signal was transmitted to two comparators which were set to detect the highest and lowest points of the wave. Each subject received 50 flashes of light at systolic and 50 flashes of light at diastolic pressure which were presented by alternating flashes at systolic and diastolic pressure in blocks of 10.3

Since the precise temporal relationship between carotid pulse pressure and baroreceptor activity is as yet unclear, it was also of interest to examine changes in AEPs associated with arteries whose pulsating activity is out of phase with the carotid artery. For this reason, pulse pressure waves were monitored from two other arteries (one cephalic and one peripheral) and AEPs were elicited during systolic and diastolic pressure recorded from both of these sites.
The cephalic artery, which was measured from the supraorbital, is only slightly (approximately 25-50 msec) out of phase with the carotid artery whereas the peripheral artery, the palmar digital artery, shows a major phase shift (approximately 150-200 msec). Because they are only slightly out of phase, it was assumed that the AEPs associated with carotid and cephalic pulse pressure waves would be very similar. On the other hand, there is a considerable time lag between carotid and digital pulse pressures, and it was speculated that the AEPs recorded at digital pulse pressures would be markedly different from those recorded at carotid and cephalic pulse pressures.

Data Reduction

Averaged Evoked Responses. Electrocortical activity associated with the 50 flashes occurring at systolic and diastolic pressure for carotid, cephalic and digital blood flow was converted from analog to digital at a sampling rate of 100 hz for a period of 500 msec following the flash. These data were then averaged and graphed using a Nova 3/12 computer system. The AEPs associated with systolic and diastolic pressure for carotid, cephalic, and digital blood flow were averaged across subjects for both hemispheres separately yielding 6 AEPs associated with the right hemisphere and 6 associated with the left hemisphere which are illustrated in Figure 9.

Three measurements were taken for each of the 12 AEPs obtained for each subject: peak delays, wave component amplitudes, and overall amplitudes. These are described in detail under Experiment I and, as in that experiment, two independent judges chose the peaks. The mean
Figure 9

Average evoked response waveforms associated with systolic and diastolic pressure for carotid, cephalic and digital blood flow.
of the interrater reliability coefficients computed for each subject was .96, indicating that the peaks were clearly represented in all but a few of the waveforms obtained.

**Results**

**Discriminant Function Analyses.** As described in Experiment I, the AEPs were analyzed using the stepwise discriminant function program provided by BMDP7M (Dixon, 1977). The points which significantly differentiated the waveforms are indicated with arrows in Figure 9 and the jackknifed classification matrices are presented in Table 1.

As is apparent in Figure 9, the differences between AEPs recorded from the right and left hemispheres are striking. In the right hemisphere, 5 points significantly differentiated the two waveforms associated with carotid pulse pressure (410, 170, 250, 90 and 180 msec in order of inclusion) whereas in the left hemisphere no points differentiated the two AEPs. The classification matrices (see Table 1) provide further evidence of the differences between the two hemispheres; the percentage of AEPs recorded from the right hemisphere that were classified correctly was relatively high whereas the percentage of correct classifications of AEPs recorded from the left hemisphere was only slightly above the level expected by chance.

The discrimination between the two waveforms associated with cephalic blood flow was also considerably better for AEPs recorded from the right hemisphere than those recorded from the left. In the right hemisphere, 14 points significantly differentiated the two waves, and the first five that entered the function (450, 210, 90,
<table>
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<th>Right Hemisphere</th>
<th>Left Hemisphere</th>
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<td></td>
<td>Systolic</td>
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<td><strong>Carotid</strong></td>
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<tr>
<td>Systolic</td>
<td>14 (77.8%)</td>
<td>4</td>
</tr>
<tr>
<td>Diastolic</td>
<td>3</td>
<td>15 (83.3%)</td>
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<td><strong>Cephalic</strong></td>
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<tr>
<td>Systolic</td>
<td>18 (100%)</td>
<td>0</td>
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<tr>
<td>Diastolic</td>
<td>0</td>
<td>18 (100%)</td>
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<tr>
<td><strong>Digital</strong></td>
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</tr>
<tr>
<td>Systolic</td>
<td>14 (77.8%)</td>
<td>4</td>
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<tr>
<td>Diastolic</td>
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250 and 170 msec in order of inclusion) were remarkably similar to the five points associated with the discrimination for the carotid pulse pressure wave. The fact that 100% of the waves recorded at systolic and diastolic pressure were classified correctly (see Table 1) emphasizes the fact that the two waveforms recorded from the right hemisphere were significantly different. In the left hemisphere, only three points differentiated the two AEPs (300, 120 and 30 msec) and the percentage of waves classified correctly was only slightly above the level expected by chance.

Whereas the AEPs associated with carotid and cephalic pulse pressure were quite similar, those associated with digital pulse pressure were notably different. Unlike AEPs associated with carotid and cephalic pulse pressures, the major differences in AEPs recorded at digital pulse pressures occurred in the left cerebral hemisphere. Several points differentiated the waveforms recorded at systolic and diastolic pressure in the left hemisphere (30, 300, 120, 230, 130, 290, 220, 330, 10, 210 and 490 msec) but only three differentiated the two AEPs recorded from the right hemisphere (80, 320 and 20 msec). In addition, all of the AEPs recorded from the left hemisphere were classified correctly whereas the percentage of cases recorded from the right hemisphere that were classified correctly was much less impressive (see Table 1).

**Analyses of Variance.** In order to clarify the findings revealed by the discriminant function analyses, the amplitudes and latencies of the individual components of the AEPs associated with each of the blood flow measures were analyzed. Three separate 2 (systolic/
analyses of variance with repeated measures of all the factors were performed for carotid, cephalic and digital pulse pressure waves.

Significant three-way interactions emerged for wave component amplitudes associated with both carotid, $F_{4,68} = 2.62, p < .05$, and cephalic pulse pressure, $F_{4,68} = 8.15, p < .01$, but not for those associated with digital pulse pressure. These interactions, illustrated in Figure 10, resulted primarily from the fact that in the right hemisphere PI was larger at diastolic pressure than at systolic pressure. Simple main effects tests revealed that in the right hemisphere PI was significantly larger at diastolic pressure than at systolic pressure recorded from both the carotid, $F_{1,17} = 4.90, p < .05$, and the cephalic, $F_{1,17} = 17.67, p < .01$, arteries. Figure 10 also illustrates that the relationships between the amplitudes of each component at systolic and diastolic pressure were identical for both carotid and cephalic pulse pressure.

There were no differences in latencies of any of the AEP components associated with carotid, cephalic or digital pulse pressure waves. Furthermore, the analyses of variance failed to reveal any significant differences in amplitudes or latencies of the AEPs associated with digital pulse pressure. In view of this, results of the discriminant function analyses of AEPs associated with digital pulse pressure should be interpreted cautiously.

The overall amplitudes of the AEP were analyzed using a 3 (pulse pressure waves) x 2 (systolic/diastolic) x 2 (hemispheres) analysis of variance with repeated measures of all the factors. There was a
Figure 10

Wave component amplitudes associated with carotid and cephalic pulse pressure.
significant interaction between systolic/diastolic pressure and hemispheres, $F(1,17) = 5.02, p < .05$, which is illustrated in Figure 11. As shown in the figure, overall amplitudes were larger in the left hemisphere when stimuli were elicited at systolic pressure than at diastolic pressure but this relationship was reversed in the right hemisphere.

**Discussion**

Changes in carotid pulse pressure are clearly related to changes in the visual evoked response. Furthermore, these changes are markedly different in the two cerebral hemispheres. In the right hemisphere, AEPs recorded during systolic and diastolic pressure were clearly differentiated from each other whereas in the left hemisphere the two waveforms were nearly identical. The differences in the right hemisphere were due primarily to the fact that P1 waves were dramatically enhanced in AEPs elicited at diastolic pressure.

The changes in electrocortical activity associated with cephalic and digital pulse pressure provide interesting evidence regarding the temporal course of baroreceptor influences on the brain. Since the AEPs associated with cephalic pulse pressure were remarkably similar to those associated with carotid pulse pressure, it appears as if the influence of the baroreceptors on electrocortical activity persists for at least 25-50 msec after stimulation. Within approximately 150-200 msec after stimulation, however, electrocortical activity undergoes a dramatic change. The changes in the right hemisphere that are associated with carotid and cephalic pulse pressure vanish. In fact,
Figure 11

Overall amplitudes for systolic and diastolic pressure in the right and left hemispheres.
the discriminant function analyses suggest that major differences appear at this time in the left hemisphere. This finding should be considered tenuously, however, since the analyses of variance did not reveal statistically significant differences in amplitudes or latencies of the two waveforms recorded from the left hemisphere at this time.

These relationships illustrate that the influence of baroreceptor activity within one cardiac cycle follows a very specific temporal course. A delay of only 150 msec completely changes the impact of systolic pulse pressure on the brain. In view of this, it is not surprising that the data regarding cardiac phase influences on behavior are equivocal. As discussed earlier, all of these studies have focused on waves of the EKG which are imprecise reflections of systolic and diastolic pressure. The results of the present study strongly suggest that robust behavioral differences will emerge when the temporal relationships are precise.

The similarities between changes in AEPs associated with carotid pulse pressure and changes associated with heart rate are striking. For example, AEPs associated with both low and high heart rate and diastolic and systolic pressure could be differentiated in the right hemisphere but not in the left (see Figures 2 and 9). In both Experiment I and the present experiment, differences in the right hemisphere were due primarily to changes in the amplitude of the P1 wave. The P1 wave was enhanced when stimuli were elicited during low heart rate and during diastolic pressure. The amplitude of the P3 wave was largest in both hemispheres when stimuli were presented during high
heart rate and systolic pressure. Finally, the overall amplitudes of AEPs were larger in the right hemisphere when stimuli were elicited at low heart rate and at diastolic pressure but larger in the left hemisphere during high heart rate and systolic pressure.

While these similarities suggest that the relationship between cardiac phase and behavior may be similar to the relationship between heart rate and behavior, there were also differences that deserve to be pointed out. First, the enhancement of P1 waves recorded at diastolic pressure was much more dramatic than that observed during low heart rate. Second, the primary component was severely diminished during low heart rate but enhanced during diastolic pressure. Finally, the amplitude of P2 was larger during low heart rate than high heart rate but smaller during diastolic pressure than systolic pressure.

These similarities and differences are interesting when viewed in terms of their behavioral implications. The evidence suggests that the behavioral effects of a change within one cardiac cycle are similar but not identical to the effects of a change in heart rate. This is consistent with studies indicating that changes in pressure and rate exert similar but different influences on baroreceptors, perhaps by stimulating sets of baroreceptors with different thresholds (see Milnor, 1974). Elucidation of the differences between the behavioral effects of changes in heart rate and changes within one cardiac cycle must await results of behavioral investigations that carefully control for the temporal factors which these results indicate are critical.
EXPERIMENT III
Influences of the Interaction Between Heart Rate and Carotid Pulse Pressure on the Visual Evoked Response

Introduction
The results of Experiment I indicated that changes in heart rate are associated with changes in electrocortical activity. In Experiment II, similar electrocortical changes were associated with the carotid pulse pressure wave. In an intact, healthy organism, however, heart rate and carotid pulse pressure do not influence the baroreceptors independently. Rather, baroreceptors are continually presented with pulsating waves of various frequencies. Changes in frequency (i.e., heart rate) coincide with changes in mean pressure, and baroreceptors encode the interaction between pulsatile and mean pressure levels.

The way that baroreceptors encode this interaction is extraordinarily complex. Within a normal range, increases in non-pulsatile blood pressure are linearly related to increases in baroreceptor firing (see Green, 1967). When subjected to pulsatile pressure, however, baroreceptors respond maximally at the peak of the pressure wave and minimally at the valleys (Ead, Green, & Neil, 1952; Heymans & Neil, 1958; Gero & Gerova, 1965). There are data to suggest that when pulsatile and non-pulsatile pressures interact, baroreceptor firing
is linearly related to the additive effects of the two (Arndt, Morgenstern & Samodelev, 1977). The situation is complicated, however, because baroreceptors have a threshold, and this linear relationship appears to hold true only above this threshold level. To add to the complexity, baroreceptors also have a saturation point, and when pulsatile and mean pressures sum to above this saturation point, their sensitivity begins to decline (Arndt et al., 1977). Since it has been impossible to determine the absolute values of the threshold and saturation points in human subjects (Arndt et al., 1977), the influence of this interaction on baroreceptors and the brain in healthy human subjects is unknown. There appear to be at least two possibilities. If mean pressure changes are above threshold and below the saturation point, pulsatile pressures would have more impact at the high mean pressures (i.e., high heart rate). If, however, mean pressure increases are above the saturation point, then pulsatile pressures would have more impact at the lower mean pressure level. There is evidence that baroreceptors operate physiologically near threshold level (Arndt, Dorrenhaus & Weicken, 1975) which argues in favor of the first prediction.

The significance of this interaction has been demonstrated not only at the level of the baroreceptors but also in psychophysiological studies. The Laceys (1974), for example, have reported that the relationship between heart rate and reaction time is significantly greater when stimuli are presented during diastole than when they are presented during systole. Following a series of studies demonstrating the influences of cardiac phase, the Laceys stated, "It is also clear
that all these (cardiac phase) effects are frequency dependent, for their magnitudes and temporal courses depend on the level of heart rate" (Lacey & Lacey, 1972). One initial speculation regarding the nature of this interaction rested on evidence (Spickler & Kezdi, 1967) that there is a "phase shift" between cardiac phase and baroreceptor firing at higher heart rate levels (Lacey & Lacey, 1974). This proposed explanation suggests that as heart rate increases, baroreceptor output is displaced forward in time changing the cardiac phase-baroreceptor relationships. Some problems with the study by Spickler and Kezdi have been pointed out, however, and more recent evidence indicates that baroreceptor discharge is not prolonged as frequency increases (Lacey & Lacey, 1978). As the Laceys have stated, the behavioral data regarding the interaction between heart rate and cardiac phases are "data in search of a theory" (Lacey & Lacey, 1978).

The following experiment was designed to examine the influence of this interaction on electrocortical activity. Although the significance of the interaction between heart rate and cardiac phase has been demonstrated at the level of the baroreceptors and evidence indicates that it is the impact of this interaction that is related to behavior, no psychophysiological investigations have been designed specifically to assess this interaction. If baroreceptors operate near threshold level as has been suggested (Arndt et al., 1975), it may be predicted that the influence of systolic and diastolic pressure will be more apparent at high heart rate than at low heart rate.
Method

Subjects

Fifteen right-handed men with the same qualifications as those who participated in Experiment I served in the experiment.

Procedure

The procedure was similar to the ones used in Experiments I and II. Fifty flashes of light were presented during each of the following four conditions: a) high heart rate/systolic pressure, b) high heart rate/diastolic pressure, c) low heart rate/systolic pressure, and d) low heart rate/diastolic pressure. The pulse pressure was always recorded from the carotid artery. As in the other experiments, the conditions were counterbalanced in blocks of 10 flashes. Heart rate, carotid blood flow, eye movements and EEG were monitored in precisely the same manner as described earlier.

Data Reduction

Averaged Evoked Potentials. The electrocortical activity associated with the 50 flashes from each of the four conditions was converted from analog to digital at a sampling rate of 100 hz for a period of 500 msec following the flash. These data were then averaged and graphed using a Nova 3/12 computer system yielding 4 AEPs for each subject for each hemisphere. As in the other experiments, peak delays, wave component amplitudes and overall amplitudes were computed for each of the 8 AEPs obtained for each subject. The methods for obtaining these measures are described in detail in Experiment I.
Heart Rate. The rates of five heart beats were recorded for each flash: two heart beats prior to the stimulus, the beat during which the stimulus occurred, and the two beats following the stimulus.

Eye Movements. As in the other experiments, trials associated with eye movements or eye blinks were repeated. No further analyses were conducted.

Results

Heart Rate. To test whether the flashes of light actually occurred at different heart rates, a 4 (conditions) x 5 (blocks) x 10 (flashes) x 5 (beats) analyses of variance with repeated measures of all the factors was performed. This analysis revealed a highly significant interaction between conditions and beats, F(12,168) = 37.31, p < .01. The mean heart rate that elicited stimuli for the high heart rate/systolic condition (75.5 bpm) was almost identical to the heart rate level for the high heart rate/diastolic condition (75.0 bpm), but these differed significantly from heart rate during the low heart rate/systolic (65.3 bpm) and low heart rate/diastolic condition (65.3 bpm).

Carotid Blood Flow, Heart Rate and the AEP. To test whether systolic and diastolic pressures had a differential effect during high and low heart rate, the AEPs associated with each of the four conditions were averaged for all subjects for both hemispheres separately. This yielded four AEPs recorded from the right hemisphere and four recorded from the left which are illustrated in Figure 12. As in the other experiments, these waveforms were analyzed using both multivariate discriminant function analyses and univariate analyses of
Figure 12

Average evoked response waveforms associated with systolic and diastolic pressure during low and high heart rate.
variance.

**Discriminant Function Analyses.** The first functions computed compared the four AEPs recorded from the right and left hemispheres separately. No points significantly differentiated the waveforms in either analysis, and neither the function generated for the right hemisphere nor the one generated for the left hemisphere was very impressive when used to classify the individual cases. The classification matrices and the plots of canonical variables revealed that this lack of significance resulted from the fact that AEPs recorded during high and low heart rate were very similar. The major differences appeared to be related to differences between waveforms recorded at systolic and diastolic pressure.

Guided by these analyses, four more discriminant functions were generated to compare the two waveforms illustrated in each quadrant of Figure 12. The points that significantly differentiated each pair of waveforms are indicated with arrows in the figure and the classification matrices are shown in Table 2.

In the right hemisphere, several points differentiated the two waveforms at both high (240, 450, 80, 10, 200 and 100 msec) and low heart rate (250, 30, 450, 190, 70, 160, 300, 20, 350, 420 and 90 msec). The classification matrices presented in Table 2 are particularly revealing since they indicate that the number of cases classified correctly was identical at high and low heart rate when stimuli occurred at systolic pressure but classification of AEPs recorded during diastolic pressure was much more successful at high heart rate than at low heart rate. These findings indicate that systolic and diastolic
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<td><strong>Right Hemisphere</strong></td>
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<td>High heart rate</td>
<td>Systolic</td>
<td>13(86.7%)</td>
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<td>Diastolic</td>
<td>0</td>
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<tr>
<td>Low heart rate</td>
<td>Systolic</td>
<td>13(86.7%)</td>
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<td><strong>Left Hemisphere</strong></td>
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<tr>
<td>High heart rate</td>
<td>Systolic</td>
<td>11(73.3%)</td>
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<td></td>
<td>Diastolic</td>
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<tr>
<td>Low heart rate</td>
<td>Systolic</td>
<td>9(60%)</td>
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pressure are clearly differentiated in the right hemisphere at both high and low heart rate, but that the differences are greater during high heart rate. The differences in AEPs recorded during high and low heart rates were due primarily to differences occurring at diastolic pressure.

As in the previous experiments, the discriminant functions for the AEPs recorded from the left hemisphere were remarkably different from those rendered from the right hemisphere. Only one point (230 msec) differentiated the waveforms (at low heart rate) and as a result, the classifications were unimpressive (see Table 2).

Analyses of Variance. Figure 13 illustrates the wave component amplitudes of the four pairs of waveforms. Four 2 (systolic/diastolic) x 4 (AEP components) analyses of variance were performed to compare the latencies and amplitudes of the waveforms shown in the figure. Only the analyses of AEPs recorded from the right hemisphere during high heart rate revealed a significant interaction between systolic/diastolic pressure and AEP components, $F(3,42) = 5.33, p < .01$. Simple main effects tests indicated that this was due to an enhancement of P1 at diastolic pressure, $F(1,14) = 18.21, p < .01$. None of the analyses revealed any differences in the latencies of any of the waves.

The overall amplitudes of the waveforms were analyzed using a 2 (heart rate levels) x 2 (systolic/diastolic) x 2 (hemispheres) analysis of variance. A significant 3-way interaction emerged, $F(1,14) = 7.98, p < .01$, which is illustrated in Figure 14. Similar to findings from Experiment II, overall amplitudes were larger in the
Figure 13

Wave component amplitudes for interactions between heart rate and carotid pulse pressure.
Figure 14

Overall amplitudes associated with the interaction between heart rate and carotid pulse pressure.
left hemisphere when stimuli were elicited during systolic pressure but larger in the right hemisphere when they were elicited during diastolic pressure.

**Discussion**

As reviewed earlier, baroreceptors do not respond to changes in pulsatile pressure and mean pressure independently in the intact healthy organism. The two interact, and it is clear from the present findings that this interaction is related to changes in the visual evoked response. Evoked responses associated with systolic and diastolic pressure can be differentiated from each other during both high and low heart rate, but the differences are more pronounced during high heart rate levels. These differences appear to be related to changes in AEPs recorded at diastolic rather than at systolic pressures. As in Experiments I and II, these findings were true only for electrocortical activity recorded from the right hemisphere. There were no significant differences among the waveforms recorded from the left hemisphere.

As discussed earlier, when pressure changes are above threshold and below the saturation point of the baroreceptors, pulsatile pressures have greater impact on firing at higher pressure levels (Arndt et al., 1977). It has been impossible, however, to determine the absolute threshold and saturation points of baroreceptors in human subjects. The fact that systolic and diastolic pressure were related to greater electrocortical changes during high heart rate than low heart rate suggests that normal fluctuations in heart rate and pulse
pressure are above threshold and below the saturation point in healthy human subjects.

One proposed mechanism of interaction between heart rate and cardiac phase has been that there is a "phase shift" between cardiac phase and baroreceptor firing during high heart rate (Lacey & Lacey, 1974). This suggests that the discrete burst of firing at systolic pressure might be delayed and occur during diastolic pressure at high heart rate levels. Another possibility, illustrated in Figure 8, is that at high heart rate, baroreceptors fire maximally at systolic pressure but do not cease firing at diastolic pressure as they do at low heart rate. Both of these possibilities suggest increased baroreceptor firing during high heart rate at diastolic pressure levels. As a result, it would be expected that differences between AEPs recorded at systolic and diastolic pressure would be greater during low heart rate than during high heart rate.

The results of the present study as well as recent studies of baroreceptor discharge patterns in cats (Lacey & Lacey, 1978) do not support this view. In fact, the findings of the present study suggest that precisely the opposite occurs: that baroreceptor discharge is diminished at diastolic pressure during periods of high heart rate. This alternative view is presented in Figure 15 and illustrates increased baroreceptor firing at diastolic pressure during periods of low heart rate. This would explain the fact that differences in AEPs recorded at systolic and diastolic pressure were more pronounced during high heart rate than during low heart rate and that these differences were related primarily to changes occurring at diastolic
Figure 15

Proposed model of the relationships between heart rate, EKG, carotid pulse pressure and baroreceptor activity.
pressure. It is conceivable that baroreceptors begin discharging to code the diastolic pressure level at low heart rate since there is a considerable amount of time between pulses. At high heart rate, however, there is little time between pulses, and baroreceptor discharge may remain minimal at diastolic pressure.

Regardless of the precise relationships between heart rate, cardiac phase and baroreceptor activity, the results of this study clearly indicate that cardiac phase and heart rate interact in their influence on cortical activity. It is therefore not surprising that some findings from behavioral studies focusing on either heart rate or cardiac phase alone are equivocal. For example, the results of the present study indicate that the influence of pulsatile pressure diminishes with cardiac deceleration. Several investigators attempting to relate cardiac phase to behavior have employed reaction time tasks with a warning signal (Thompson & Botwinick, 1970; Delfini & Campos, 1972) and it is well known that a warning signal leads to marked cardiac deceleration (Graham & Clifton, 1966; Lacey & Lacey, 1970; Lacey, 1972). The behavioral effects of changes in cardiac phase may disappear in this situation as a result of the marked cardiac deceleration, which would account for the fact that several studies using reaction time tasks with a warning signal to investigate cardiac phase-behavior relationships have not yielded significant results (Thompson & Botwinick, 1970; Delfini & Campos, 1972), whereas those not using a warning signal have reported significant relationships (Saari & Pappas, 1976; Sandman et al., 1977). Furthermore, the results of the present study suggest that influences of heart rate
may be dependent upon cardiac phase. Because of the instrumentation in Experiment I, stimuli almost always occurred precisely at the onset of the R wave of the EKG and clear differences emerged between evoked responses recorded at low and high heart rate. In the present study, however, AEPs were recorded only at diastolic and systolic pressure, and no clear differences emerged between AEPs recorded at high and low heart rate.

Changes in heart rate and cardiac phase do not influence baro-receptors or behavior independently in the intact organism. Consistent with this notion, the results of the present study indicate that these two types of changes interact in their influence on electrocortical activity. As pointed out earlier, baroreceptors are distributed throughout the body, and there seems little reason to assume that they influence the brain independently. The findings of the present study suggest that it is these complex patterns of afferent autonomic activity that relate to the brain and behavior rather than single events. The relationship between various patterns of autonomic activity and behavior has only begun to be explored (see Schwartz, 1976).

**General Discussion**

The impact that stimuli exert on the brain differs markedly at various levels of heart rate and carotid pulse pressure. Both primary and secondary components of the AEP change as heart rate and carotid pulse pressure change. Furthermore, these changes follow a precise temporal course and differ significantly in the two cerebral
hemispheres. This set of findings emphasizes the fact that the cardiovascular system does not merely serve an effector function. Afferent impulses from the cardiovascular system have effects beyond those classified as homeostatic.

The fact that changes in the cardiovascular system were related to significant changes in the primary component of the AEP in each experiment emphasizes the significance of these cardiovascular events. The primary component is thought to represent direct impulses travelling from the receptor organ to the cortex and is believed to be related to the characteristics of the stimulus rather than of the organism (Lindsley, 1969; Beck, 1975). As a result, the primary component has been termed the "exogenous component" (see Beck, 1975; Donchin, McCarthy & Kutas, 1977) and is rarely studied by investigators who are interested in psychological processes. The results of the present studies clearly indicate that changes in the organism do affect the primary response. Since this component has been associated with the earliest sensory events, it appears as if changes in the cardiovascular system are related to the act of sensation at a much earlier stage than has previously been thought.

The secondary components have been termed "endogenous components" and have been related to various psychological processes (see Beck, 1975; Donchin et al., 1977). Positive peaks occurring 100 and 200 msec after the stimulus, for example, have been associated with simple perceptual processes and attention (Chapman & Bragdon, 1964; Donchin & Cohen, 1967) and may involve "the selection of a particular input channel to be examined" (Beck, 1975). In the present studies, the
positive peak 100 msec after the flash was significantly enhanced during low heart rate, at diastolic pressure recorded from the carotid artery, and at diastolic pressure during periods of high heart rate. These findings provide neurophysiological evidence that is remarkably consistent with formulations from behavioral studies suggesting that decreases in baroreceptor firing are related to the facilitation of sensory intake (Lacey, 1967).

It is intriguing that in each experiment these relationships differed in the two cerebral hemispheres. The two hemispheres are specialized for different types of cognitive style with the left related to logical, analytical abilities and the right to a more holistic, spatial, nonlogical mode of thinking (see Sperry, 1974 for a review). In each of the present studies, the overall amplitudes recorded from the left hemisphere were largest during high heart rate and systolic pressure and smallest during low heart rate and diastolic pressure. Since both the right hemisphere (Dustman et al., 1976) and transient bradycardia (Lacey, 1967) have been related to attentional processes and the left hemisphere (see Donchin et al., 1977) and brief hypertensive states (Lacey, 1967) have been related to cognitive processing, it seems possible that the cardiovascular system influences behavior by differentially stimulating the hemispheric structures.

There are several physiological processes and anatomical considerations which may play a role in this lateralization. First, the heart is not a symmetrical organ and there are anatomical differences between the right and left carotid arteries. The left common carotid branches directly from the aortic arch whereas the right common carotid
does not; it branches from the subclavian artery which connects directly with the aortic arch. Although the innervation of the right and left carotid sinuses appear to be similar, the innervation of the aortic arch is clearly lateralized, and there are baroreceptors situated in the aortic arch as well as in the carotid sinuses. The left vagus nerve has terminals on the aortic arch, but the right vagus nerve passes across the subclavian artery and descends to the trachea without branching to the aortic arch (see Netter, 1962). Impulses from the baroreceptors in the aortic arch, therefore, may be transmitted via the left vagus nerve to the nucleus tractus solitarius where the fibers cross and ascend to the right cerebral cortex. In this way, the contribution of the impulses from baroreceptors situated in the aortic arch could account for the pronounced changes in the right cerebral hemisphere. Finally, baroreceptor impulses transmitted to the nucleus tractus solitarius are closely associated with activity in the reticular activating system and there is evidence to suggest that activity in this region can influence the two cerebral hemispheres differently (Starzl & Magoun, 1951; French, 1960).

The differences between the two hemispheres may also be related to changes in cerebral blood flow. In Experiment I, changes in heart rate were associated with changes in cephalic blood flow. These changes were consistent with evidence indicating that when baroreceptors are stimulated, arterial blood pressure falls which may lead to decreases in cerebral blood flow and neuronal inhibition (Purves, 1972; Ponte & Purves, 1974). Ingvar and his colleagues have demonstrated specific changes in regional blood flow that are associated with
various types of mental activity and electrocortical changes (Ingvar, 1971; Ingvar, 1972; Ingvar & Lassen, 1975; Ingvar, 1977), and there are clear differences in patterns of regional blood flow in the two hemispheres while subjects perform various tasks (Risberg, Halsey, Wills & Wilson, 1975). Thus, it seems possible that the electrocortical changes in the present studies were related to hemispheric differences in regional blood flow that were associated with the task.

Most of the experiments demonstrating the relationship between cardiovascular activity and behavior have been correlational in nature. As a result, the significance of this relationship has been a source of controversy. While the Laceys have maintained that increases in blood pressure are part of an inhibitory or restraining process which is behaviorally significant, other explanations have been offered. One view (Elliott, 1972; Hahn, 1973; Obrist, 1976; Obrist et al., 1969) stresses the correlation between somatic and cardiac activity and postulates that somatic and cardiac responses are linked and controlled by the central nervous system in parallel. This model suggests that certain processes in the brain control cardiovascular and somatomuscular activity simultaneously and that changes in behavior associated with cardiovascular activity are a result of this central controlling mechanism.

In light of this controversy, the results of the present set of experiments are particularly interesting. They indicate that changes in the cardiovascular system are not merely indices of somatomuscular activity. Furthermore, it appears as if cardiovascular changes may actually reflect and influence adaptive behavior. While it seems
possible that cells in the brain that control heart rate also influence cortical activity, there are very few cells in the brain that have been found to fire at a cardiac rhythm (Humphrey, 1967; Smith & Pearce, 1961) and it is unknown whether these changes are represented cortically. The explanation is even less viable when considered in light of evidence that the carotid pulse pressure as well as the interaction between heart rate and pulse pressure are associated with similar electrocortical changes. The moment that the carotid pulse pressure wave reaches its peak is determined by the pumping action of the heart and the dynamic activity of the carotid artery. Thus, a more likely explanation of these results is that changes in the cardiovascular system influence cortical activity.

As discussed earlier, our basic conceptions of the role of the autonomic nervous system stem historically from Cannon's notion of "fight or flight" reactions. As a result, the vast majority of psychophysiological studies have been designed to examine autonomic responses that occur as a function of psychological events. The present studies emphasize that this view of the significance of autonomic activity is incomplete. The role that the cardiovascular system plays is not completed when it responds to commands from the brain. Rather, the afferent impulses influence the brain and continually change the context with which the brain receives and processes information. In this way, behavior is determined by a complex series of interchanges between autonomic and central nervous system activity. Although this neo-Jamesian view of the organism has received its broadest support from studies of the cardiovascular system, there seems little reason to
assume that the cardiovascular system is unique in this respect.
Because it has been found that stimulus probability can influence cortical evoked responses (Squires, Donchin, Herning, & McCarthy, 1977), the number of seconds between flashes occurring at high, midrange, and low heart rate were compared. This analysis revealed that there were significantly fewer seconds between flashes at midrange heart rate than during high or low heart rate (p < .05), but that there were no differences between flashes occurring at high and low heart rate.

These percentages were obtained using a jackknifing classification procedure provided by BMDP7M (Dixon, 1977). Using this procedure, each case is classified using a discriminant function that was computed without that individual case. This method provides a completely independent replication of a study without gathering more data (John, 1977).

Differences in the number of seconds between flashes for stimuli occurring during systolic and diastolic pressure were analyzed using a 3 (blood flow measures) x 5 (blocks) x 2 (systolic/diastolic) x 9 (times) analysis of variance. No significant differences emerged; the average intertrial time was 2.65 seconds.

Differences in the intertrial intervals for stimuli occurring during the 4 different conditions were analyzed using a 5 (blocks)
x 4 (conditions) x 9 (times) analysis of variance. There were no significant differences; the average intertrial time was 6.76 seconds.
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