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AUGMENTATION OF THE AUDITORY EVENT RELATED POTENTIALS OF THE BRAIN DURING DIASTOLE

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Previous studies demonstrated that stimuli synchronized with systolic and diastolic phases of the pulse pressure wave enhanced the visual event related potentials (ERPs) of the brain. The present study extended these observations to the auditory ERP in passive and attentional conditions. Pure tones were synchronized with systolic and diastolic phases of the cephalic and palmar arteries. During one condition, subjects were paid a bonus for reporting accurately the number of times they heard a tone (attention condition) and in a second condition they listened passively (non-attend). Stimuli synchronized with the diastolic phase, reliably produced augmentation of the N1 component across all conditions. The N2 component was smaller in the right hemisphere of attentive subjects when stimulation was synchronized with diastole. These results were discussed in the context of the cognitive psychophysiology proposed by Pieton and Hillyard (1974).

INTRODUCTION

In a number of studies, the Lacey's found that tasks which required attention to the environment reliably resulted in heart rate deceleration. Conversely, heart rate accelerated during tasks requiring "rejection of the environment" or cognitive elaboration (Lacey, 1959; Lacey et al., 1963; Lacey, 1967; Lacey and Lacey, 1974). Furthermore, enhanced performance of tasks requiring attention has been reported when stimuli were synchronized with low heart rate or with early components of the ECG (Sandman et al., 1977; Saari and Pappas, 1976; Birren et al., 1963). Performance of tasks requiring decision-making was facilitated when stimuli were triggered by elevated heart rate (Sandman et al., 1982). Finally, learned control of the heart can have systematic influences on behavior since tachistoscope stimuli presented during reinforced decelerated heart rate were perceived more accurately than when they were presented during increased heart rate (McCanne and Sandman, 1974). Conversely, reinforced heart rate acceleration was reliably related to increased counter-arguments in a study of persuasion (Cacioppo et al., 1978) and the perception of aversive stimuli (Shapiro and Reeves, 1982).

Among the most compelling evidence for relations between the brain and the cardiovascular system were the studies of Bonvallet et al. (1954). Essentially these investigators demonstrated that activation of baroreceptors of the carotid sinus exerted an inhibitory influence on cortical activity. Mechanical distension of the wall of the carotid sinus, an analogue of increased pressure, changed electrocortical activity from low-voltage fast, to high-voltage slow wave activity (Bonvallet et al.,

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1954) and inhibited evoked monosynaptic reflexes (Svensson and Thoren, 1979).

Recent studies have demonstrated that heart rate and the systolic and diastolic components of the pulse pressure wave influenced the averaged event-related potentials (ERPs) of the brain. During decelerating heart rate (Walker and Sandman, 1979) and the diastolic components of the pulse pressure wave (Walker and Sandman, 1982; Sandman et al., 1982) the P1 and P2 components of the visual ERP were augmented. Conversely, presentation of stimuli synchronized with accelerating heart rate or with systolic components of the pulse pressure wave had a suppressive influence on the visual ERP. The major influence of the cardiovascular system in these studies, were in ERPs measured from the right hemisphere of the brain.

The current study was conducted to pursue further these findings using the auditory ERP. Further, in the present study, the possible influence of attentional demands was assessed by having the subjects either passively listen (non attend) or to listen, count and report (attend) the number of stimuli they detected. This procedure is known to influence the early components of the auditory ERP (Picton and Hillyard, 1974), but the effects of this procedure on the cardiovascular relationship with the ERP are unknown.

METHOD

Subjects

Eighteen right-handed, healthy volunteers were paid \$10 to participate in the study. All subjects were between the ages of 19 and 30 years and none reported loss of auditory acuity. Subjects were screened for evidence of high blood pressure, cardiovascular pathology or other major medical problems. Eleven of the subjects were women and 7 were men.

Procedure

Subjects reclined in a comfortable chair while transducers were applied for recording EEG from each hemisphere of the brain and pulse pressure waves from the supraorbital artery and the palmar digital artery of the non-preferred hand. White noise from speakers in the subject's cubicle saturated the room to mask extraneous noise. Low-level illumination, provided by a DC source was sufficient to view the subject via a closed circuit television system from the control room. An intercommunication system permitted continuous auditory monitoring of the subject. The subjects were fitted with headphones (Senheisser HD 400) for auditory stimulation. Pure tones (450 Hz) were synchronized with either systolic or diastolic components of the pulse pressure wave recorded from the supraorbital or digital artery.

The subjects were tested in two different conditions. In one condition, they were instructed to relax and passively listen to the stimulus (non-attend condition); in the second condition they were instructed to count the stimuli and report the result at the end of the session (attend condition). A \$2 bonus was offered for accurate performance to induce greater attention to the task. The order of presentation of these sessions was balanced. In both conditions the subjects were instructed to keep their eyes closed. The subjects received 40 artifact-free stimuli for each ERP generated (a total of 8 ERPs were collected for each subject). An automatic artifact detection procedure was effective in aborting trials with high frequency or high amplitude signals.

Apparatus

Physiological recordings were obtained with a Grass. Model 79 polygraph equipped with appropriate preamplifiers and driver amplifiers. The peaks and valleys of the pulse pressure waves were detected by Schmidt triggers and delivered to a Digital PDP 11/34 computer to initiate the averaging epoch. On-line averaging of the ERP provided a refreshed, running average as well as the EEG sample from which the average was computed. The computer rejected all samples with frequencies greater than 100 Hz or amplitudes over 100 μ V.

EEG electrode placement. Grass cup Ag–AgCl electrodes were attached to the scalp above the right and left hemisphere of the brain according to the International 10–20 system. Monopolar placements at C3 and C4 were referenced to linked mastoids. The electrode sites were swabbed with

acetone and the electrodes filled with Grass EEG cream and affixed to the scalp with Collodion. Pairs of electrodes with impedance of greater than 10.000 Ω were replaced. Electrodes with differences between the left and right hemisphere of greater than 1000 Ω were corrected. The EEG signal was amplified by Grass AC preamplifiers with the low frequency filter set at 1 Hz and the high frequency filter set at 35 Hz.

Pulse pressure wave. Plethysmographs containing light-emitting diodes and narrow band emitting infrared radiation with a wave length of 0.74 μ m were placed over the supraorbital notch (just temporal of the nasium) and the palmar digital artery (the third phalange of the ring finger). The signal was amplified by the Grass AC preamplifier with a time constant of 0.08 s and a half amplitude high frequency filter of 15 Hz.

Data analysis

The ERP was analyzed by sampling the EEG at 1 kHz for 640 ms. The sampling period was initiated by detection of systole or diastole of either the supraorbital or palmar arteries. A 500 ms sampling period was zeroed by averaging a 140 ms prestimulus epoch. For each point of the ERP an average and variance was obtained.

The ERP data was subjected to two different analyses. First, with the 1 kHz sampling rate, the prominent peaks, within prescribed latencies, of the ERP (P1, N1, P2, N2, P3) were identified and their amplitudes (peak-to-peak) and latencies recorded with an automated procedure. These data were formatted to automatically enter into the BMD statistical package (P2V). Each data point (the 5 different amplitudes and latencies) was subjected to analysis of variance. The second analysis required that the data points of the ERP were smoothed by calculating the average of each 10 succesive points. The resulting 100 Hz resolution was used for analysis in the Stepwise Discriminant Function program (BMD P7M).

RESULTS

The data for the ERP were examined with a 2 $(attend/non-attend) \times 2$ (left/right hemisphere of

the brain) $\times 2$ (cephalic/digital plethysmograph placements) $\times 2$ systole/diastole) repeated measure analyses of variance. Supplementary analyses for the attend condition were computed to determine the difference between subjects who correctly or incorrectly identified the number of stimuli. A final analysis was performed on the inter-heart-beat intervals for the heart period before, during and after presentation of the stimulus.

Amplitude measures

Stimuli presented during the diastolic component (10.31 μ V) of the pulse pressure wave elicited a significantly larger ($F_{1,17} = 12.48$, P < 0.01) response than presentations during systole (8.88 μ V) for the earliest negative wave of the ERP (N1). A significant 4-way interaction ($F_{1.17} = 13.57$, P <0.001) is illustrated in Fig. 1. The most reliable effect is the pervasive influence of systole/diastole on the ERP since presentation of stimuli during diastole yields a larger N1 component across all conditions. Less apparent aspects (i.e. failing to reach statistical significance) of the interaction are the greater differences between systole and diastole during the attend condition in the right hemisphere, especially for the cephalic placement, There were no other effects on the amplitude of the ERP due to presentation during systole or diastole



Fig. 1. The amplitude of the N1 component of the ERP is augmented when stimuli are synchronized with diastolic phases of the pulse pressure waves.

P1 latency

The interaction of attend/non-attend and systole/diastole was statistically significant ($F_{1,17} =$ 4.84, P < 0.04) for the latency of P1. The latency was shortest when stimuli were synchronized with diastole in the attend condition. There were no effects related to systole/diastole on the latency of other components of the ERP.

Correct / incorrect responders: amplitude

Consistent with the previous analyses, the influence of cardiac phase on the amplitude of the N1 component (systole = 8.70 μ V; diastole 10.80 μ V) was highly significant ($F_{1,12} = 10.34$, P < 0.01). This pervasive influence of phase is illustrated in Fig. 2. A significant influence ($F_{1,12} = 16.15$, P < 0.01) of cardiac phase also was detected for the N2 component of the ERP. However, the influence of stimuli synchronized with systole or diastole on this later component was reversed from that observed with N1. For the N2 component, stimuli synchronized with systole resulted in a larger response (18.91 μ V) than stimuli presented during diastole (17.69 μ V).

A 3-way interaction among hemisphere, cardiac phase and group (correct/incorrect) was statistically significant ($F_{1,12} = 5.19$, P < 0.04) for the N2 component and is illustrated in Fig. 3. The most reliable finding was that the inattentive (incorrect) subjects had larger N2 components than attentive (correct) subjects. Stimuli synchronized with diastole generally elicited smaller N2 responses than stimuli evoked by systole, especially for the subjects correctly identifying the number of stimuli (attentive subjects). Further, this effect was most apparent in the right hemisphere. These later two trends were not significant by tests of simple effects. Overall, the differences between systole and



Fig. 2. The amplitude of N1 is augmented when stimuli are synchronized with diastole across every experimental condition. The magnitude of effect appears greatest in the attentional condition.



Fig. 3. The amplitude of N2 is suppressed when stimulation is synchronized with diastole. The effect is especially pronounced in the right hemisphere of attentive subjects.

diastole were greatest in the right hemisphere for both attentive and inattentive subjects.

NI latency

The latency of the N1 was significantly shorter ($F_{1,12} = 7.48$, P < 0.02) in subjects who correctly identified the number of stimuli (98.09 ms) compared with subjects responding inaccurately (110.00 ms). Stimuli synchronized with diastole (340.05 ms) produced significantly ($F_{1,12} = 8.17$, P < 0.01) shorter latencies for the P3 component than stimuli synchronized with systole (363.63 ms).

Stepwise discriminant analysis

The results of the stepwise discriminant analysis are summarized in Table I. Essentially, in every analysis except for measures in the left hemisphere



Fig. 4. Smoothed ERPs averaged across all subjects illustrating (with arrows), in 10 ms increments, the points on the wave from which discriminant function analysis are detected are the best predictors of difference. Negative is graphed down.

	Non-attend		Attend		Jack-knifed only	
	Classification	Jack-knifed	Classification	Jack-knifed	Correct	Incorrect
Right systole	75.0	75.0	81.2	68.7	100	71.4
Right diastole	81.2	68.7	67.5	62.5	100	85.7
Left systole	81.2	75.0	68.7	62.5	85.7	57.1
Left diastole	81.2	75.0	62.5	62.5	85.7	57.1

Classification matrix for discriminant analysis of ERPs collected during systole and diastole in attend and non-attend conditions

in subjects who were incorrect, the ability to separate the ERPs collected during systole and diastole was statistically significant. Further, as presented in Fig. 4, the components occurring around N1 were the best predictors of differences among diastole and systole. Unlike studies of visual ERP, there were no major differences between the left and right hemisphere with this analysis. In the



Fig. 5. The smoothed ERPs for attentive (correct) and inattentive (incorrect) subjects. The major influence is the relative suppression of the N2 component in the right hemisphere during diastolic stimulation. Negative is graphed down.

TABLE I

non-attend condition, the influence of systole and diastole were statistically reliable in the left ($F_{5,26} = 2.87$, P < 0.05) and right $F_{5,26} = 2.92$, P < 0.05) hemispheres. In the attend condition, the differences were also reliable (left; $F_{5,26} = 3.68$, P < 0.05) (right; $F_{5,26} = 3.0$, P < 0.01) even though the classifications were somewhat inferior to the non-attend condition.

Perhaps the most interesting finding is the difference between attentive and non-attentive subjects. For the attentive subjects, the separation between systole and diastole was highly significant (right, $F_{5,8} = 9,68$, P < 0.01; left, $F_{5,8} = 8.34$, P < 0.01). However, in the inattentive subjects the ability to discriminate systole and diastole was much poorer and was no better than chance in the left hemisphere (Fig. 5).

Inter-heart-beat interval

The influence of early (systole) and late (diastole) stimulation in the cardiac cycle on heart period was examined. The heart period before, during and after stimulation is illustrated in Fig. 6. The interaction between cardiac phase and ordinal heart beat was significant ($F_{2,28} = 3.68$, P < 0.04). The heart period was extended during stimulation for both systole and diastole, however, stimulation during systole resulted in a larger period. Conversely, stimuli synchronized with diastole extended the heart period of the beat after stimula-



Fig. 6. The heart period before, during and after stimulation early (systole) and late (diastole) in the cardiac cycle. Prolongation of the heart period was evident for early and late stimulation of the ongoing period but only late stimulation prolonged the subsequent cycle.

tion. Thus, consistent with the finding of the Lacey's (1967), stimuli administered early in the cardiac cycle extended the heart period of the subsequent beat.

DISCUSSION

In a paradigm nearly identical with the current study, Sandman et al. (1977) reported that tachistoscopic stimuli were perceived more accurately when they were synchronized with decelerating heart rate or the P wave of the ECG. The findings of the present study are consistent with this earlier report as well as later reports (Walker and Sandman, 1979, 1982; Sandman et al., 1980; Sandman et al., 1982) of the influence of the cardiovascular system on the visual ERP. In the present study stimuli synchronized with diastole, reliably resulted in a larger N1 component of the ERP compared with ERPs synchronized with systole. This effect was pervasive and remained robust across all experimental and subject categories. Although robust changes were observed in the N1 component as a function of stimulus synchronization with different phases of the cardiovascular system, there was no effect on P2. This disassociation suggests that the physiological mechanisms subserving N1 and P2 portend unique, functional significance and invites further study.

Attenuation of N2 was observed in attentive subjects especially when stimulation was synchronized with diastole, the optimal cardiovascular parameter for sensitivity to external stimulation. This result appeared most reliably in ERPs recorded from the right hemisphere, a finding consistent with the laterality of ERPs in tasks of attention (Dustman et al., 1976) and with previous reports of right hemispheric susceptibility to cardiovascular influences (Walker and Sandman, 1979, 1982; Sandman et al., 1982; Sotaniemi, 1980).

The significance of these findings may be obvious when reviewed within the cognitive psychophysiology proposed by Picton and Hillyard (1974). These authors argued that the increased N1-P2 complex reflected facilitation of stimuli by focussing attention to particular "channels" or to dimensions of stimuli (Broadbent, 1970). Hence, selectivity of perception was enhanced by the ability of the perceiver to reject irrelevant information based upon categorical (i.e. "channeled") comparisons. Although Picton and Hillyard did not differentiate the N1 from the P2 in their earlier analysis, more recent data indicates that protracted negativity (Nd) with its onset at N1 best reflects selective attention (Hansen and Hillyard, 1983). The N2 component was believed to be discretely influenced by the subject's state of alertness. Specifically, N2 is attenuated in alert subjects, during widespread cortical activation, and may relate to optimizing sensitivity to external stimulation (Posner and Boies, 1971).

The N1 component (related to selective attention) of the ERP was most sensitive to the influence of cardiovascular synchronization with external stimuli, but reliable effects on N2 (related to arousal) were also detected. Specifically, stimulation synchronized with diastole agumented N1 and attenuated N2. These findings support the proposal that a continuum of attention may be modulated by the covariation of the cardiovascular system and the brain (Lacey, 1967).

These data suggest that awareness of the environment is partially regulated by the interactions of the brain and the heart. Although it is probable that many visceral and somatic systems "tune" the brain via their afferent pathways, the results of the present study provide direct information of this "tuning" by the cardiovascular system. One speculative conclusion implied by these findings is that a modest portion of environmental awareness or attention is "hardwired". For instance, with a task chosen purposefully for its simplicity, a reliable influence on the ERP was observed. Even when attentional demands were imposed, or in subjects who either were "attentive" or "inattentive" the same effect on the ERP was evident. Thus, a portion of the variance (10–20% based on the present data) relating to attention (Sandman et al., 1977), or to components of the ERP, may be accounted for by peripheral physiological systems (or any "background" activity) which may be inviolably linked to the brain.

Another speculative conclusion derived from these data is that there are optimal physiological "windows" for enhancing perception or attention and that these windows are cyclic. Certainly, the data from the present study and others (Sandman et al., 1977; Saari and Pappas, 1976; Birren et al., 1963; Walker and Sandman, 1979; 1982) indicate that there are precise periods during the cardiac cycle or the carotid pressure gradient that optimize perception and the impact of stimulation on the brain. Indeed, the classical findings of Bonvallet et al. (1954) indicated that mechanical analogues of increased pressure resulted in characteristic patterns of EEG activity. However, only a marginal influence of the cardiovascular system on the brain is observed in the absence of external stimulation (Sandman et al., 1982; Walker and Walker, 1983). The possibility that the brain is pulsed by the cardiovascular system (Kennedy, 1959: Sandman, O'Halloran and Isenhart, 1984) cannot be dismissed. It is also conceivable that the "window" of optimal performance is the result of either fortuitous or purposeful synchrony among physiological systems. Although resolution of this causeand-effect question must be deferred, the findings clearly indicate that there are cyclic physiological states which modulate the impact of external stimuli.

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