Pre-ejection Period: Measuring Beta-adrenergic Influences Upon the Heart

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ABSTRACT

Increasing interest among psychophysiologists in sympathetic (beta-adrenergic) influences upon the heart has created the need for noninvasive techniques for assessing these influences. The validity of pre-ejection period (PEP), a systolic time interval, as a measure of beta-adrenergic influences upon myocardial contractility is evaluated. Details of a procedure for determining PEP using a polygraph and digital computer are presented. This methodology is then applied to an experiment in which the intracardiac (PEP) and arterial subintervals of pulse transmission time (PTT) are measured during biofeedback-assisted control of PTT in order to evaluate the relative contribution of changes in PEP to PTT control.

DESCRIPTORS: Pre-ejection period, Beta-adrenergic cardiac influences, Contractility, Pulse transmission time.

There has been considerable recent interest among psychophysiologists in measures which reflect beta-adrenergic influences upon the heart (Lawler & Obrist, 1974; Heslegrave & Furedy, 1979). This interest stems in part from the theoretical position of Obrist and his colleagues (Obrist, Webb, Sutterer, & Howard, 1970), which suggests that heart rate (HR) may come under either vagal or sympathetic (beta-adrenergic) control depending on situational factors. According to this view, HR change in most experimental conditions is mediated primarily by alterations in vagal restraint rather than sympathetic drive, and is associated with concomitant somatic activity (Obrist et al., 1970). However, under certain stressful experimental conditions, HR increases may come under beta-adrenergic control and may be unrelated to changes in somatic variables (Obrist, Lawler, Howard, Smithson, Martin, & Manning, 1974). Since measurement of HR alone does not indicate whether vagal or beta-adrenergic influences are prepotent, a number of other cardiovascular measures have been proposed to enable this differentiation.

Additional interest in beta-adrenergic measures stems from recent suggestions that excessive sympathetic drive is important in the early stages of essential hypertension (Julius & Esler, 1975; Weiner, 1977), and that increases in cardiac contractility tend to precede myocardial infarctions by approximately six months (Theorell & Rahe, 1975). Further, the use of pharmacological beta-adrenergic blockade has been proposed as a treatment for anxiety patients (Granville-Grossman & Turner, 1966).

The focus of this paper will be on pre-ejection period (PEP). PEP, a systolic time interval, is a noninvasive cardiological measure which reflects cardiac contractility, a function which is primarily controlled by beta-adrenergic mechanisms. PEP has not been employed previously in psychophysiological research. This paper briefly reviews characteristics of PEP which are relevant to its utility and validity in psychophysiological research, and describes the measurement of PEP in a computer-based psychophysiology laboratory. Finally, an experiment is reported in which the systolic time interval methodology is used to measure the intracardiac (PEP) and arterial subintervals of pulse transmission time (PTT) during biofeedback-assisted control of PTT.

PEP as a Beta-adrenergic Measure

The primary systolic time intervals are PEP, left ventricular ejection time (LVET), and electromechanical systole (EMS). PEP extends from the electrocardiogram (ECG) Q-wave (the onset of ventricular depolarization) to the initial point of ejection of blood from the left ventricle which is demarcated by the opening of the aortic valve. PEP is composed of the electrical-mechanical delay which occurs between the onset of depolarization and the beginning of ventricular contraction, and the isovolumic contraction time during which the left ventricle is contracting prior to the opening of the aortic valve. PEP therefore represents the total duration of the electrical and mechanical events prior to ejection. LVET is initiated by the opening of the aortic valve (the end-point of PEP) and is terminated by the closing of the aortic valve, thus encompassing the period during which blood is actually pumped from the left ventricle. EMS is simply PEP plus LVET, the total time of electrical and mechanical components of systole.

There is considerable empirical validation of PEP as an indirect measure of myocardial contractility. Ahmed, Levinson, Schwartz, and Ettinger (1972) correlated PEP between subjects at rest with invasive measures of cardiac contractility and ventricular performance. They found that PEP was negatively correlated with the Frank-Levinson index of contractility ($r = -.82$) and the velocity of the contractile element ($r = -.79$) in a sample of 14 normal subjects and 14 cardiac patients without valve disease, shunts, or pulmonary-related ventricular problems. Lower magnitude correlations were found for ventricular performance measures (ejection fraction: $r = -.67$; cardiac index: $r = -.53$). The authors concluded that PEP is determined primarily by the contractile state of the heart, and is influenced by preload and afterload to a lesser extent than other performance measures.

Ahmed et al. (1972) also examined the relationship between PEP and invasive measures of contractility in response to inotropic stimuli (i.e. those which affect myocardial contractility). Isoproterenol, a drug with potent beta-adrenoreceptor activating properties, produced large magnitude decreases in PEP accompanied by large changes in contractility (measured by the Frank-Levinson index and the velocity of the contractile element).

There is also considerable empirical validation of PEP as a measure of beta-adrenergic influences upon the heart. This is consistent with the fact that contractility is primarily controlled by beta-adrenergic influences. Harris, Schoenfeld, and Weissler (1967) found that beta-blockade with propranolol eliminates the normal shortening of PEP in

response to isoproterenol. Similarly, they found that infusions of both adrenaline and noradrenaline, drugs which also activate beta-adrenergic receptors, decrease PEP. In addition, Cousineau, Lapointe, and de Champlain (1978) found circulating catecholamine levels at rest to be highly negatively correlated with PEP between-subjects ($r = -.83$).

The relationship between PEP and HR is also known. PEP is decreased and HR is increased by positive inotropic agents and adrenergic cardio-stimulation; however, PEP is unchanged by vagal blockade and atrial pacing (Harris et al., 1967), both of which do affect HR (cf. Lewis, Leighton, Forester, & Weissler, 1974; Salcedo & Siegel, 1976; Spodick & Zambrano, 1974). Thus, there is considerable evidence supporting the conclusion that PEP is specifically sensitive to beta-adrenergic influences upon the heart, in contrast to HR which responds to both sympathetic and parasympathetic influences.

Factors which Limit Interpretation of PEP

Although evidence has been reviewed that PEP reflects beta-adrenergic influences upon the heart, other factors may potentially obscure this relationship in psychophysiological research. These factors include 1) ventricular preload, 2) afterload, 3) alpha-adrenergic influences on contractility, 4) non-adrenergic drugs which affect PEP, and 5) cardiac abnormalities. We will describe the effects of each of these factors briefly and include references to more extensive discussions for the interested reader.

Preload

Preload refers to the amount of ventricular filling which occurs during diastole. Increased diastolic filling stretches the myocardial fibers and reflexively elicits increased contractility (the Frank-Starling mechanism). Thus, increased preload decreases PEP, although no beta-adrenergic influences are involved. It should be noted that the Frank-Starling mechanism acts to compensate for increased preload by increasing transfer of blood from the venous to arterial side of the heart, thus inherently decreasing preload (Berne & Levy, 1977). The existence of this compensatory mechanism suggests the need for research concerning the importance of preload effects in typical conditions encountered in psychophysiological research.

Afterload

Afterload (i.e. aortic diastolic pressure) is the load against which the left ventricle contracts. Left ventricular pressure must exceed aortic diastolic pressure in order for the aortic valve to open. Thus,

increased afterload prolongs PEP because it takes longer for ventricular pressure to rise above aortic pressure. It follows that changes in peripheral resistance which affect diastolic blood pressure can be expected to influence PEP independent of beta-adrenergic control.

There are two lines of evidence which suggest that afterload effects may not be critical for the use of PEP in typical psychophysiological conditions. Obrist, Light, McCubbin, Hutcheson, and Hoffer (1979) found inconsistent and generally nonsignificant correlations between diastolic blood pressure (which estimates aortic diastolic pressure) and PTT (which encompasses PEP) with sympathetic innervation intact (median $r = -.12$) and blocked by propranolol (median $r = -.01$). Cousineau et al. (1978) failed to find a significant difference in PEP between normotensives and diastolic hypertensives, suggesting that chronically elevated afterload does not produce chronic PEP increases.

Alpha-adrenergic Influences on Contractility

The possibility of alpha-adrenergic influences on contractility was raised by Harris et al. (1967) who found that PEP *increased* in response to adrenaline and noradrenaline infusion following beta-adrenergic blockade. Lewis et al. (1974) attributed this effect to alpha-adrenergic stimulation which produces reflexive vagal effects on contractility. However, the existence of evidence that contractility is not affected by direct vagal stimulation (Carlstein, Folkow, & Hamburger, 1957), and that vagal blockade with atropine has no effect on PEP (Harris et al., 1967), casts doubt upon Lewis et al.'s hypothesis of a vagal link between alpha-adrenergic stimulation and changes in contractility.

Non-adrenergic Drug Effects

Several non-adrenergic inotropic drugs such as digitalis and glucagon markedly decrease PEP (Harris et al., 1967; Spodick & Zambrano, 1974). In addition, angiotensin increases PEP, apparently because of its potent vasoconstrictive properties (Harris et al., 1967). Clearly, PEP cannot be interpreted in terms of beta-adrenergic influences on the heart when these agents have been administered.

Cardiac Abnormalities

Extreme caution must be exercised when interpreting PEP in subject populations with cardiac abnormalities. These considerations are reviewed elsewhere (Lewis et al., 1974; Salcedo & Siegel, 1976; Spodick & Zambrano, 1974).

Other Noninvasive Beta-adrenergic Measures

Several measures other than PEP have been employed in psychophysiological research which may be specifically sensitive to beta-adrenergic influences on the heart. In contrast to PEP, they are uncalibrated, and are not meaningful in between-subjects comparisons. These measures will be described briefly, but thorough examination of the validity of each measure is beyond the scope of this paper.

Carotid dP/dt Ratio

Obrist et al. (1974) have utilized a measure of cardiac contractility which employs the maximum positive slope of the differentiated carotid pulse (dP/dt). This measure was later changed (Obrist, Gaebelein, Shanks-Teller, Langer, Grignolo, Light, & McCubbin, 1978; Light & Obrist, Note 1) to a ratio measure of maximum ascending slope divided by the slope at the dicrotic notch on the descending pulse wave. Carotid dP/dt responses are blocked by propranolol (Obrist et al., 1978) and significant correlations of dP/dt and PTT have been reported (Obrist et al., 1979).

An additional carotid slope measure has been used in cardiological research which involves a different method of quantification from that used by Obrist et al. The ratio of the maximum ascending carotid slope to the difference between the maximum ascending slope and maximum descending slope (which occurs immediately prior to the dicrotic notch) is correlated $-.75$ with PEP between subjects (Kahn & Spodick, 1972). Movement artifact is a common problem with the carotid slope measures (Obrist et al., 1974).

PTT

A second indirect measure of contractility used by Obrist et al. (1979) and Light and Obrist (Note 1) is PTT, the interval from the ECG R-wave to the carotid, temporal, or radial pulse. PTT encompasses most[1] of PEP, but is uncalibrated because it also includes the arterial transit time of the pulse wave. Measuring PTT from the R-wave to a pulse transducer on the ear provides greater freedom from artifact than other recording sites (Obrist et al., 1979). PTT is discussed more extensively below.

T-wave Amplitude

Heslegrave and Furedy (1979) and Matyas and King (1976) have summarized evidence supporting the interpretation of the amplitude of the ECG T-wave as a beta-adrenergic measure. T-wave amplitude is not in use in the cardiological literature as a measure of sympathetic cardiac influences, and no correlative studies with other beta-adrenergic measures are available. Further validation research

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[1] Since PEP is initiated by the Q-wave and PTT by the R-wave, PTT encompasses all of PEP except the Q-R interval.

is needed before T-wave amplitude can be accepted as a beta-adrenergic measure.

Measurement of the Systolic Time Intervals

Because PEP is new to the psychophysiological literature, we will describe a technique for determining PEP with maximum artifact rejection in a computer-based psychophysiological laboratory. The computer program we employ operates on a PDP-11 minicomputer with 16K memory in real time, although the same principles would apply to off-line analysis of recorded signals.

In most applications, PEP is determined by subtracting LVET from EMS because of difficulties in determining the initial point of ejection noninvasively. LVET can be measured on a peripheral pulse because the temporal relationship between ejection and valve closure is preserved in the pulse pressure wave as it travels away from the heart (Spodick & Zambrano, 1974). This peripheral pulse may be detected at the carotid artery (Spodick & Zambrano, 1974), the finger (Chirife, Pigott, & Spodick, 1971), or the pinna of the ear (Chirife & Spodick, 1972). Determination of LVET in our laboratory utilizes detection of the pulse at the ear because of its relative freedom from movement artifact (Chirife & Spodick, 1972; Quarry-Pigott, Chirife, & Spodick, 1973; Haffty, Kotilainen, Kobayashi, Bishop, & Spodick, 1977). This pulse is detected by differentiating the signal from an ear densitogram (a photoplethysmographic device); we will refer to this differentiated signal as DD. The pulse upstroke of the DD (indicating the opening of the aortic valve and onset of ejection) will be referred to as DDu, and the incisural notch (indicating the closure of the aortic valve and end of ejection) will be referred to as DDn.

Determination of the three primary systolic time intervals (PEP, LVET, and EMS) requires locating four points in time: the ECG Q-wave, DDu, heartsound S2 (the sound of aortic valve closure), and DDn. Although S2 and DDn refer to the same mechanical event, DDn is delayed by the duration of pulse travel to the ear. This interval, S2–DDn, is the true transit time (TT) of the pulse wave from the heart to the ear.

The locations of these four points are illustrated in Fig. 1. Apparatus requirements and algorithms for computerized detection of the points are discussed below.

Q-wave

The apparatus requirements for detection of the ECG Q-wave are not critical as long as the Q-wave is clearly distinguishable on the polygraph record. The ECG signal depicted in Fig. 1 was obtained using Beckman miniature electrodes in a bipolar
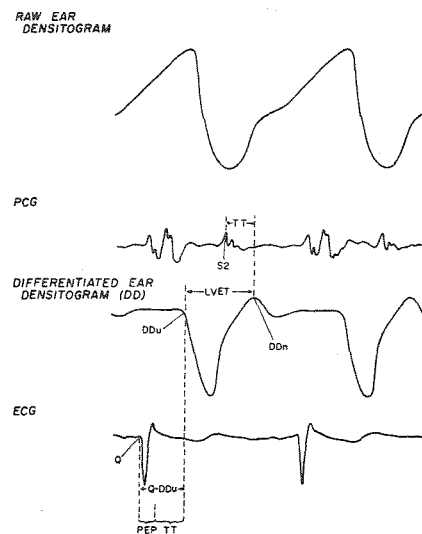

Fig. 1. Sample polygraph record depicting points which demarcate the systolic time intervals. Note that PEP is determined by subtracting TT (actually measured between S2 and DDn) from Q–DDu. The raw ear densitogram signal is illustrated for comparison purposes but is not used to measure the systolic time intervals. (Paper speed: 100 mm/sec. All signals are displayed positive down except PCG which is displayed positive up.)

configuration. The two electrodes were placed on either side of the chest midway between the waist and shoulders. Other electrode placements which emphasize the Q-wave can also be used.

The algorithm for detecting the Q-wave initiates a timer at the last ascending point within 60 msec of a "valid" R-wave (one which occurs within ±400 msec of the mean interbeat interval of the previous trial).

DDu and DDn

The ear densitogram raw signal is transduced with a Hewlett-Packard #780-16 photoelectric ear-piece attached to the pinna of the right ear. The differentiated signal (DD) is obtained using a differentiator circuit (National Semiconductor, 1975) with a 100 Hz corner frequency. The low frequency filter on a Grass 7P5B AC Preamplifier is adjusted between .15 and 1 Hz to provide a sharp negative spike corresponding to the incisural notch on the raw signal (see Fig. 1). Obtaining a sharp DD signal often requires moving the transducer slightly to place it over a small artery.

DDu is located using an algorithm to detect positive slope which we have found to be insensitive to the amplitude of the DD signal and baseline shift. This algorithm places DDu at the foot of the positive DD wave. The interval is rejected as artifactual if Q–DDu is more than 50 msec less than the Q–DDu

mean from the previous trial, or if it is more than 100 msec longer.

DDn is determined as the most negative point (the nadir) of the DD with the condition that the DD wave does not reverse direction within 50 msec. The DDu–DDn interval is rejected as artifactual if it is more than 50 msec less than the DDu–DDn interval from the previous trial, or if it is more than 100 msec longer.

S2

Apparatus requirements for accurate detection of S2 are relatively critical because of placement and artifact problems with the phonocardiogram (PCG). In our laboratory, the PCG signal is obtained with a heartsounds microphone (Narco Biosystems #705-0016) attached to the fifth intercostal space (approximately 1–2 in. below the left nipple) with an elastic strap. PCG is amplified with a 7P5B AC Preamplifier with 10 Hz high pass filtering. The microphone must be situated such that a very sharp, high amplitude initial S2 wave is obtained. This often requires moving the microphone slightly to find the best S2 signal, particularly with obese subjects.

The computer algorithm for locating S2 on the PCG signal uses a digital averaging procedure analogous to that used in average-evoked-potential research. The PCG is sampled at a high rate during a 100-msec period (centered on the DDu–S2 interval from the previous trial), and then averaged over 60 successive heart beats. Assuming relatively steady-state conditions, the signal (i.e. the initial S2 spike) is amplified while random artifactual noise is cancelled.

At the end of 60 beats, the averaged PCG is scanned using an algorithm to locate the largest positive wave (S2), and the average S2–DDn interval is calculated. The averaged PCG is then displayed on an oscilloscope with a pointer indicating the computed S2 in order to confirm that a satisfactory S2 signal has been obtained.

The following intervals are directly measured during each cardiac cycle: 1) Q–DDu, 2) DDu–DDn (LVET). The following intervals are arithmetically derived at the end of each trial: 1) TT = S2−DDn, 2) PEP = mean Q−DDu interval minus TT, 3) LVET = mean DDu−DDn interval, 4) EMS = PEP plus LVET. Note that PEP is derived by subtracting TT from mean Q−DDu because DDu represents the ejection point (the end-point of PEP) delayed by TT, the time it takes the pulse to travel to the ear. As noted above, we use this procedure for trial lengths of 60 beats, although shorter lengths are possible depending upon the quality of the PCG signal.

Effective artifact rejection in this system depends upon the use of criteria for identifying the various waveforms and strict criteria for rejecting waveforms as artifactual if they fall outside certain expected time "windows." Since these windows are adjusted on the basis of previous trials, the program is able to track large baseline changes in the systolic time intervals while maintaining consistent artifact rejection. There are four separate opportunities for rejecting artifactual data on each beat, and all intervals are rejected for that beat if any point is not in its proper place. In practice, few beats are rejected unless the subject moves about vigorously, and artifact rejection is quite complete.

Several other computer programs for detection of the systolic time intervals have been reported (Divers, Katona, Dauchot, & Hung, 1977; Kyle & Freis, 1971; Swatzell, Bancroft, Macy, & Eddleman, 1973). They are designed for cardiological applications in which the subject is at complete rest, and are not applicable in psychophysiological research in which the subject is involved in a behavioral task or is being stressed. In contrast to the program we have described, these systems use the carotid pulse rather than the DD to locate the initiation and termination of ejection. We use the DD because it is subject to much less artifact than the carotid pulse, and has actually been used for systolic time interval measurement (hand-scoring) during bicycle exercise (Quarry-Pigott et al., 1973). These programs also attempt location of S2 on every beat, an approach which is impractical unless the subject is at complete rest. The averaging procedure we use allows location of S2 over selected trial lengths, and provides cancellation of artifactual noise in the PCG signal.

The primary disadvantage of the system presented above is that it does not allow calculation of PEP on every beat. This is not a problem with studies in which steady-state conditions can be reasonably assumed over the period of a trial. However, this disadvantage limits the usefulness of the program for detecting short-term responses (i.e. phasic changes which occur within two or three heart beats) to discrete stimuli.

An Application of Systolic Time Interval Methodology

As previously noted, PTT, extending from the ECG R-wave to the arrival of the pulse wave at the radial artery, encompasses most of PEP. Since variation in PTT has been interpreted by some authors in terms of change in blood pressure (Steptoe, Smulyan, & Gribbin, 1976) or by others in terms of changes in myocardial contractility (Obrist et al., 1979), we conducted a biofeedback experiment in which the contribution of PEP changes to feedback control of PTT could be directly assessed.

PTT was proposed by Steptoe et al. (1976) as an indirect measure of mean arterial pressure. Steptoe

et al. reported individual correlations of PTT with mean arterial pressure ranging from $-.45$ to $-.85$ (median $r = -.60$) during Valsalva maneuver, mental arithmetic, and isometric handgrip. Following this validation work, Steptoe (1976, 1977a, 1977b, 1978; Steptoe & Johnson, 1976) interpreted successful control of PTT simply as blood pressure control in a series of biofeedback studies.

Using slightly different methodology, Obrist et al. (1979) evaluated the relationship between PTT and systolic blood pressure during stressful tasks. They reported individual correlations of PTT with systolic blood pressure ranging from $-.49$ to $-.93$ (median $r = -.85$) with intact sympathetic innervation and using a surface transducer to detect the radial pulse. Obrist et al. interpreted PTT primarily as a measure of myocardial contractility, and the close relationship between PTT and systolic blood pressure was attributed to common influences of contractility on both measures.

Using the median correlations reported by Steptoe et al. (1976) and Obrist et al. (1979), it may be estimated that blood pressure changes (or factors common to both measures) account for 36% to 72% of the variance in PTT, ranging from 20% to 80% of the variance for individual subjects. These data suggest that, at least for some subjects, PTT is not determined wholly by variation in blood pressure. In addition, these estimates are based upon relatively large magnitude changes in PTT and blood pressure produced by laboratory stressors. It is possible that blood pressure covaries to a lesser degree with the more modest PTT changes typically found in a biofeedback task. Although correlative data has implicated blood pressure as a partial determinant of PTT (Steptoe et al., 1976; Obrist et al., 1979), the contribution of changes in myocardial contractility to variation in PTT has not been directly assessed. Obrist et al. (1979) reported substantial correlations between carotid dP/dt and PTT (median $r = -.66$). Further, sympathetic blockade (with propranolol) virtually eliminated PTT responses to stress. These findings indicate a relationship between contractility and PTT. However, the systolic time interval methodology would allow direct assessment of the contribution of PEP changes to variation in PTT.

PTT is composed of two subintervals: the interval from the R-wave to ejection (this interval will be referred to as PEP[2]), and from ejection to the peripheral pulse (TT[3]). Validation work by Grib-

bon, Steptoe, and Sleight (1976) suggests that TT is influenced by arterial pressure. Gribbin et al. artificially manipulated arterial transmural pressure while recording transit time between two pulses on one arm. All correlations between arterial pressure and transit time were $-.90$ or greater. Thus PTT may reflect both arterial pressure (because it encompasses TT) and cardiac contractility (because it encompasses PEP).

The purpose of the present experiment was to measure separately the subintervals of PTT in order to evaluate the individual contributions of PEP and TT to PTT change. We employed a three session procedure using a PTT biofeedback task similar to that used by Steptoe (1976, 1977a, 1977b, 1978).

Method

Subjects

Eight male subjects were recruited by a classified advertisement offering "$2.00 per hour for subjects in a Psychology experiment." The subjects were all undergraduate students.

Apparatus

The apparatus used was described above in relation to measurement of the systolic time intervals. To enable measurement of PTT to the finger[4], a Grass PTT1-6 finger plethysmograph was attached to the index finger of the right hand and covered with a black mitten (to eliminate 120 Hz noise from overhead lighting). This signal was amplified using a 7P5A Preamplifier with 1 Hz high pass filtering.

The PDP-11 minicomputer controlled beat-by-beat feedback of PTT. The feedback consisted of a light-emitting diode (LED) numerical display placed in front of the subject at eye level. On "blood pressure" increase trials, msec change in PTT from the preceding trial mean plus 110 was displayed following each beat; on decrease trials, the display consisted of the msec change from baseline subtracted from 90. Thus, decreased PTT from baseline (i.e. increased blood pressure or contractility) resulted in an increased display, and increased PTT (i.e. decreased blood pressure or contractility) resulted in a decreased display. Visual feedback was continuous during feedback trials, and the display was blank during baseline trials. Direction of attempted change was indicated by a second LED display in the subject chamber which remained illuminated during feedback trials.

Procedure

After the subject was seated in a comfortable chair and transducers were attached, he was given written instructions explaining that he was to try to increase or decrease his "blood pressure" when cued by the second display, and that changes above or below 100 on the feedback display would reflect successful increases or decreases in his blood pressure. In order to increase motivation, sub-

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[2]Note that PEP as it is used here excludes the Q-R interval, which is normally included in PEP. This change was made in order to simplify terminology. The Q-R interval was measured separately.

[3]TT as it is used here refers to the transit time to the radial artery or finger. Note that TT was also used above to refer to the transit time to the ear in relation to the systolic time intervals.

[4]PTT was measured using a photoplethysmographic transducer on the finger in order to make it comparable to Steptoe's procedure, while at the same time avoiding artifact problems associated with a radial transducer.

jects were informed that they would earn 1¢ for each msec change in the PTT trial mean they produced on each feedback trial, and that this amount would be displayed at the end of the trial. Finally, the subjects were asked to "breathe normally and avoid physical movement" during the experiment.

Following a 5-min adaptation period, the first baseline trial was initiated. The experiment consisted of an alternating series of 8 baseline trials of 60-beat duration (feedback display blank) and 8 feedback trials of 180-beat duration (continuous feedback). Increase and decrease trials were in randomized order. The cumulative amount of money earned was shown on the second display for 5 sec at the end of each feedback trial.

The second and third sessions, scheduled within a period of one week, were identical to the first.

Trial means for the following dependent physiological measures were computed and stored on-line: interbeat-interval in msec (IBI); PEP; TT to the finger; and LVET.

Results[5]

Physiological dependent measures were submitted to repeated-measures analyses of variance (ANOVAs) with Direction of attempted change (increase vs decrease), Session, Control (baseline vs feedback trial), and Repetition (four repetitions of each direction per session) as within-subject factors. Significant Direction × Control interactions for PTT, $F(1/16)=10.4$, $MS_e=36.9$, and TT, $F(1/16)=6.1$, $MS_e=17.2$, indicated that subjects were able to significantly decrease PTT from baseline by -2.8 msec (means = 251.0 and 248.1; $t(6)=4.9$), but were unable to increase it (means = 251.3 and 250.5; $t(6)=1.4$).

Examination of the results for individual subjects during attempted PTT decrease naturally revealed a range of individual differences in the magnitude of PTT decrease. Since the average PTT decrease for all 8 subjects was small, and meaningful evaluation of the contribution of PEP changes to PTT changes first requires successful control of PTT, we subjected the data from our 4 best PTT decreasers to additional descriptive analyses. Statistical tests were not performed because of the low N. Note in Table 1 that these 4 subjects decreased PTT by an average of -5.5 msec, consisting of a PEP decrease (i.e. increased contractility) of -2.4 msec, and a TT decrease (i.e. increased arterial pressure) of -3.3 msec.

Among these 4 subjects, IBI decreased -58.3

[5]The .05 level of significance was employed for all statistical tests.

TABLE 1

Physiological data for 12 PTT decrease trials
(4 best subjects)

Measures[a]	Means (msec) (SDs in Parentheses)		Change
	Baseline	Feedback	
PTT	252.6 (19.2)	247.1 (20.5)	-5.5
TT	154.6 (17.1)	151.3 (17.0)	-3.3
PEP	98.3 (23.1)	95.9 (24.2)	-2.4
IBI	839.5 (96.9)	781.2 (99.2)	-58.3

[a]In this table PTT and PEP are initiated by the R-wave; PTT and TT are measured to the finger.

msec, LVET decreased -4.2 msec, and the Q–R interval was essentially constant.

Discussion

Subjects significantly decreased PTT with feedback, and the TT changes which accompanied this control were significant. However, change in PTT overestimated the actual magnitude of change in TT because of changes in PEP. Although PEP changes were not significant using data from all subjects (many of whom showed little or no feedback control of PTT), the contribution of PEP to PTT decreases in the 4 most successful subjects was over 40%. This suggests that examination of changes in PEP may be particularly advisable in subjects who exhibit the best control of PTT.

These results raise important questions concerning the interpretation of PTT. Unless the subintervals of PTT are measured, there is little basis for determining whether PTT changes are due to changes in myocardial contractility or blood pressure (or both). Direct measurement of PEP facilitates this determination, as well as providing a transit time measure (TT) which reflects only arterial components.

These results are preliminary evidence that PTT control reflects changes in both PEP and TT, although data from a larger number of subjects who show large magnitude PTT control is needed to confirm this observation. Caution should be exercised when interpreting PTT control simply as blood pressure control in a biofeedback paradigm. Work is now in progress in our laboratory in which the subintervals of PTT are evaluated during laboratory stressors in order to apply the same type of analysis to PTT changes in response to stress.

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