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Methodology

Measuring Baseline-Treatment Differences in Heart Rate Variability: Variance versus Successive Difference Mean Square and Beats per Minute versus Interbeat Intervals

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ABSTRACT

It is argued that: if linear trends are present in heart rate (HR) data, due to sinus arrhythmic variation and the gradual nature of the HR response to an external treatment, the time-series statistic successive difference mean square (SDMS) will be a logically more appropriate estimate of HR variability than is variance. A fifty-subject study assessed both the empirical import of this argument as well as the question of the appropriate scale of measurement, i.e., either beats per minute (BPM) or interbeat intervals (IBI). Separate analyses to determine changes in HR variability from baseline to treatment conditions were carried out using each combination of statistic and scale to define HR variability. These analyses showed that HR variability either did not change or was significantly decreased by the treatment depending on the combination of statistic and scale used to define HR variability. This differential result, depending on the type of analysis, was due to the fact that nonrandom linear trends in the HR data spuriously inflated variance relative to SDMS and affected the BPM scale significantly more than the IBI scale. The major result from this study is that the combination of SDMS as the variability statistic, and IBI as the scale of measurement for HR, is both the best and most appropriate technique for assessing changes in HR variability. In addition, the IBI scale should be considered when analyzing mean HR scores if differential linear trends exist between conditions being compared, as in this case, since the IBI scale should increase statistical precision for detecting differences between mean HR scores during those conditions. Finally, when the more appropriate SDMS statistic and IBI scale define HR variability, this study supports the claims of previous investigators who have reported that increases in cognitive functioning led to decreases in HR variability.

DESCRIPTORS: Heart rate, Heart rate variability, Variance, Successive difference mean square, Beats per minute, Interbeat intervals, Transformation, Heart rate variability changes during mental arithmetic, Mental arithmetic, Time-series statistics.

Psychophysiologists concerned with developing unobtrusive but maximally sensitive indices of cardiac function have commonly employed heart rate (HR) as a preferred measure. However, there exists a major difference between HR and other psychophysiological measures, namely that in HR time is included as a necessary component of each indi-

The first and third authors of this paper are grieved to report that the second author, who was the statistical mainstay of this work, died in November 1978, thus ending a fruitful and extensive career in which he collaborated not only with us but also with many other members of the Toronto department for over 20 years; we all miss him.

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vidual datum, whereas in other measures time is included only when it is necessary to consider response topography.[1] The particular method by which time should be included in the HR measure of cardiac function, however, has been in dispute by several investigators (Graham & Jackson, 1970; Jennings, Stringfellow, & Graham, 1974; Khachaturian, Kerr, Kruger, & Schachter, 1972; Thorne, Engel, & Holmblad, 1976). The conventional manner of including time has been to transform the time between beats, i.e., interbeat intervals (IBI), into beats per constant unit time, i.e., beats per minute (BPM). This type of BPM data transformation has been defended on historical, pragmatic and statistical grounds (Graham & Jackson, 1970). However, others have criticized this position. For example, it has been argued that BPM averaging produces errors in estimating the actual mean for a given period while IBI averaging does not result in such errors (Thorne et al., 1976). Still others (Jennings et al., 1974; Khachaturian et al., 1972) have criticized the use of the BPM scale on the basis that the reciprocal transformation of IBI to BPM is nonlinear, which results in equivalent IBI changes becoming distorted on the BPM scale with this distortion becoming serious at extreme HR values. Also, in contrast to the suggestion by Graham and Jackson (1970), these two papers have pointed out that the BPM scale does not offer any statistical advantages over the IBI scale, i.e., it does not normalize skewed and kurtotic distributions. Although there are some differences in terms of the skewness and kurtosis of BPM and IBI distributions, these differences do not seem to be great when the subject population is within the normal adult human range, but do become more important and tend to favor the IBI scale of measurement at more extreme HR values. However, this BPM-IBI controversy is an empirical rather than a logico-theoretical, statistical problem, and although the present study provides further data on which to judge the merits of each scale of measurement, this empirical BPM versus IBI issue is not the principal focus of this paper.

Our central concern is with HR *variability* changes rather than the more commonly studied *mean* HR changes between conditions, since the less thoroughly examined former measure has recently become of interest to investigators studying such areas as the psychophysiological effects of attention and cognitive functioning on the cardiac HR response (Lacey, 1967; Porges, 1972; Porges & Raskin, 1969; Walter & Porges, 1976). These studies have provided some support for the view that attention-demanding tasks requiring information processing to various degrees produce some stabilization of HR or a decrease in HR variability, with variability usually measured in terms of variance (e.g., Porges, 1972) or log variance (e.g., Walter & Porges, 1976). However, variance, or some transformation of variance, may not be the appropriate, or optimum, measure of variability in most psychophysiological experiments, and this paper will argue and present evidence for the position that another measure of variability is more appropriate.

To assess the appropriateness of the variance statistic for measuring HR variability, a commonly employed psychophysiological experimental paradigm involving HR and HR variability was used where the effect produced by a treatment on a given trial is compared with a given baseline. During the trial, nonrandom (in the sense of a lack of independence between successive beats) HR fluctuations occur because of the introduction of some external treatment or stimulus. Since the treatment-induced maximal HR change is not instantaneous, there is a gradual systematic change in HR over the course of the treatment period. In fact, studies have shown that the cardiac HR response (in a special group of subjects; Varni, Clark, & Gidden, 1971), and other measures like the electrodermal skin potential response (Leiderman & Shapiro, 1962), yield significant nonrandom trend effects due to the introduction of an external stimulus. Thus significant nonrandom trends likely exist in HR measurements during treatment periods. However, HR differs from other measures in terms of the background variability during the baseline period. With the electrodermal skin potential measure for example, the fluctuations during baseline are spontaneous in the sense that the potential at one point in time, N, is relatively independent of the potential at a point in time immediately preceding it, N−1. On the other hand, HR varies nonrandomly in a pattern referred to as sinus arrhythmia,

[1]Response topography is typically involved when the interest is in within-treatment comparisons rather than in comparing baseline and treatment periods. In particular, the typical change of interest in such within-treatment comparisons is a phasic short-term response elicited by some stimulus such as a novel stimulus (yielding an orienting reaction which, in HR, is deceleration), a US like shock in an aversive classical conditioning experiment (yielding a UR which, in HR, is acceleration), or a CS (yielding, in HR, a biphasic CR composed of acceleration followed by deceleration, at least under appropriate-duration CS-US interval conditions). Such single-period HR changes are excluded from consideration in the present paper, which is restricted to instances where the concern is always with between-treatment (i.e., more than one treatment) differences. Briefly, however, and as will be argued in more detail elsewhere, it appears that the problems due to trends discussed in the present paper would not alter the results in the case of single-period, stimulus-elicited phasic HR responses using traditional techniques of analysis.

primarily due to the influence of respiration (Guyton, 1971). As will be detailed below, the conventional measures of HR variability are spuriously altered depending on the extent to which baseline and treatment sources of variation differ from random variation.

In order to examine the effects of these potential sources of nonrandom trends on HR variability and on the different scales of measurement, i.e., BPM and IBI, the potential effects of nonrandom trends on the variance statistic and on its relationship to the population parameter must first be understood. Sample variance ($s^2=\Sigma(x_i - \bar{x})^2/(n-1)$) is an unbiased estimate of the population variance (σ^2), assuming a random sample of observations. However, s^2 does not take into account the temporal order of the observations so it is susceptible to time-dependent nonrandom trends. The degree to which nonrandom trends exist in time-series data like HR directly influences the magnitude of s^2, so that if significant nonrandom trends exist, s^2 can no longer be considered an unbiased estimate of σ^2 since the random sample assumption has been violated. For example, the effects of a gradual shift in HR on s^2 would be to increase s^2 relative to σ^2 thus making s^2 an increasingly poorer estimate of σ^2 as the HR variation becomes less random and more systematic (Bennett & Franklin, 1954; von Neumann, Kent, Bellinson, & Hart, 1941). If the degree of nonrandom trend during baseline and treatment periods is different, then the degree of error introduced into the variance measure would also be differential and any reported changes in variability between baseline and treatment periods (e.g., Walter & Porges, 1976) may be spurious. The empirical size of the potential error in assessing differences in variability by the use of s^2 is examined in this study by comparing s^2 with another measure, namely the successive difference mean square (SDMS), which minimizes the effects of gradual, nonrandom trends (von Neumann et al., 1941). This measure was originally developed in the early 1940's (Hart, 1942; von Neumann, 1941; von Neumann et al., 1941; Williams, 1941; Young, 1941) and received more attention later from Bennett and Franklin (1954), but it has seen little use (Leiderman & Shapiro, 1962; Varni et al., 1971) in standard psychophysiological studies where time-series observations are of particular significance. The SDMS statistic is defined as follows (Bennett and Franklin, 1954):

$$\delta^2 = \frac{\sum_{i=1}^{n-1} (x_{i+1} - x_i)^2}{n-1}$$

where i represents the temporal order of the observation x_i. The SDMS thus takes into account the order of the observations and is also an unbiased estimate of σ^2 with the relationship $E(\delta^2)=2\sigma^2$, therefore $\delta^2/2$ should equal s^2. The major difference between s^2 and $\delta^2/2$ is that the latter minimizes the effects of nonrandom gradual trends, which spuriously inflate s^2, and specifically removes the effects of linear trends. This study will examine the effects of nonrandom variation in HR data during baseline and treatment periods. If HR variation is essentially random or even if HR variation is nonrandom but does not include a linear component, then $\delta^2/2$ will be approximately equal to or greater than s^2 (Bennett & Franklin, 1954, p. 678) and there will be no advantage to the $\delta^2/2$ measure of variability. In fact the use of $\delta^2/2$ may prove to be disadvantageous (Burdick, 1972). If, on the other hand, linear trends are present to a significant degree, s^2 will be significantly inflated relative to $\delta^2/2$ and $\delta^2/2$ will provide a better estimate of variability than the spuriously inflated s^2 measure. Of course, if linear trends are present to a different degree in the baseline and treatment periods, the s^2 measure will be inextricably confounded.

The major purpose of this paper is to examine the effects of nonrandom (linear) trends from baseline and treatment periods on the usual measure of variability, i.e., s^2, by comparing s^2 with $\delta^2/2$, remembering that under random conditions the two statistics should be equivalent. An additional aim is to determine whether there are differential effects of such trends on the two scales of measurement, i.e., BPM and IBI, as might be expected (Burdick, 1972). The method of contrasting these variability statistics and scales of measurement was to compare baseline and treatment periods where the treatment period was known to produce a reliable biphasic (accelerating and then decelerating) HR response. Finally, this study will further examine the effects of an attention-demanding, cognitive task on HR variability in terms of the hypothesis that such increases in cognitive activity should reduce the variability of HR (Porges, 1972; Porges & Raskin, 1969; Walter & Porges, 1976). This further examination is especially critical if nonrandom, linear trends significantly influence the variance measure and if these trends are differentially present during baseline and treatment. Such an outcome would jeopardize the conclusions of previous studies on HR variability since those cited studies used the variance statistic to assess baseline-treatment differences in variability.

Method

Subjects

Fifty subjects were volunteers from an Introductory Psychology course at the University of Toronto. All subjects were healthy and free of cardiac and cardiovascular ailments by their self-reports.

Procedure

The data for this study were gathered from an experiment unrelated to the discussion in this paper (see Furedy & Heslegrave, 1977). Each subject in this experiment received 20 trials, each of which were comprised of: a 10-sec baseline period prior to each trial, a 5-sec interval during which the subject listened to the numbers for the task, and a 20-sec task or treatment period. The intertrial intervals were randomly varied among 40, 50, and 60 sec. The task consisted of the subtraction of a two-digit number from a four-digit number, which were presented verbally to the subject over headphones, followed by the serial subtraction of that two-digit number from each successively obtained difference (e.g., 2811−16). The subject was instructed to respond verbally with as many subtractions as possible in the 20-sec period which was terminated by the onset of a green light directly in front of the subject. The pairs of numbers for the task were changed for each trial. The analysis of mean HR changes showed that subjects responded with a strong biphasic acceleration-deceleration HR response.

Heart rate was continuously monitored through Ag/AgCl recording electrodes containing EKG electrolytic paste as a conducting medium between the body surface and the electrodes. The two recording electrodes were placed bilaterally on the rib cage with the reference electrode securely fastened to the subject's neck. This configuration provided a good signal for all subjects. The signal from the subject went through an E & M Biosystems Biotachometer (Model BT-1200) and was converted on a beat-by-beat basis to BPM and then displayed on an E & M Physiograph (Model Four-A). The biotachometer BPM output was then quantified by sampling, on a sec-by-sec basis, the analogue signal from the physiograph.

The quantified BPM output was transformed by the equation IBI=60,000/BPM to produce the data for subsequent IBI analyses. In order to make baseline and treatment periods comparable in terms of HR variability, the 20-sec treatment period was separated into two 10-sec periods. Thus HR variability (s^2 and $\delta^2/2$) was calculated on each scale (BPM and IBI) for the 10-sec baseline and each of the two 10-sec treatment periods. In addition, all HR variability scores were transformed by a natural log transformation which generally stabilizes the variances of these variability scores (Bartlett, 1947). This transformation also makes the variances of the variability scores comparable for the BPM and IBI scales and allows for the comparison of all factors based on within-scale difference scores even though between-scale comparisons on raw (rather than difference) scores are confounded. This point will be presented in more detail during the results.

Results

The data used in the present experiment were meant to evaluate the prediction from the cognitive activity-cardiac variability hypothesis that treatment HR variability decreases, relative to baseline HR variability, if the treatment involves an increase in cognitive activity by a method such as the performance of an arithmetic task. These data for each subject consisted of four mean log HR variability measures, one for each combination of variability statistic (s^2 and $\delta^2/2$) and scale (BPM and IBI) averaged over the 20 trials, for the baseline and treatment periods.

Fig. 1 shows the change in mean log HR variability during treatment for each combination of statistic and scale. It can be seen that different conclusions regarding the cognitive activity-cardiac variability hypothesis would be reached depending on the statistic and scale used to define HR variability. Separate ANOVAs were carried out on each of the four types of HR variability measures to determine whether HR variability was significantly altered by the introduction of a treatment which increased the amount of cognitive activity required. The results revealed that the decrease in HR variability was significant only when HR variability was measured using the s^2-IBI combination ($F(2/147) = 3.81$, $MS_e = .898$) and the $\delta^2/2$-IBI combination ($F2/147) = 6.27$, $MS_e = 1.071$). Subsequent multiple comparisons revealed no significant differences between the two treatment periods as measured by the s^2-IBI or $\delta^2/2$-IBI combinations of statistics and scales.

The differential results reported above raise the problem of which definition of HR variability provides the most reliable result. If gradual, linear trends are present to different degrees during the baseline and treatment periods and differentially affect the BPM and IBI scales, the logically most appropriate analysis involves the $\delta^2/2$ statistic and the scale least affected by gradual, linear trends.

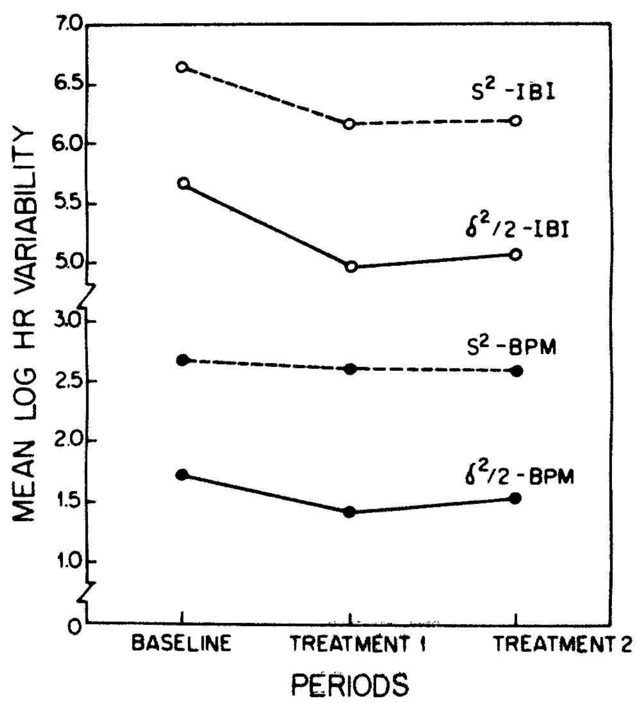

Fig. 1. Changes in mean log HR variability over periods as defined by each combination of statistic (s^2 and $\delta^2/2$) and scale (BPM and IBI).

However, if other types of trends are present, such as beat-by-beat high-low-high-low cycling, $\delta^2/2$ may be more confounded than s^2 (Bennett & Franklin, 1954; Burdick, 1972), so that s^2 and the scale least affected by these types of trends may be the preferable statistic and scale. To ascertain whether any nonrandom trends are present, an analysis was conducted using log s^2 minus log $\delta^2/2$ difference scores for baseline and the two treatment periods, and for the BPM and IBI scales. This difference score analysis is necessary in order to adequately compare the BPM and IBI scales in terms of the effects of trends. The effects of trends can be determined by comparing the two statistics since gradual, linear trends are expected to spuriously inflate s^2 while leaving $\delta^2/2$ relatively unaffected. However, inherent magnitude differences between the BPM and IBI scales make it impossible to compare these two scales directly, so difference scores are necessary to make the comparison between statistics within the same scale.

Fig. 2 shows the results of this log s^2 minus log $\delta^2/2$ difference score analysis. In order to demonstrate that gradual linear trends are present in these data and that these trends spuriously inflate s^2, the resulting mean difference scores in the figure were tested for each period and scale against the expected difference score of zero, which should result if only random variation is present in these data. These comparisons showed that for all periods s^2 significantly exceeded $\delta^2/2$ on both the IBI (baseline, $t(49)=26.09$; treatment 1, $t(49)=26.55$; treatment 2, $t(49)=31.73$) and BPM (baseline, $t(49)=26.25$; treatment 1, $t(49)=27.09$; treatment 2, $t(49)=31.98$) scales. From these results it is clear that significant nonrandom linear trends exist in baseline and treatment periods and that these trends spuriously inflate s^2 relative to $\delta^2/2$ and exceed any influence from competing cyclic trends which could make s^2 a preferable statistic.

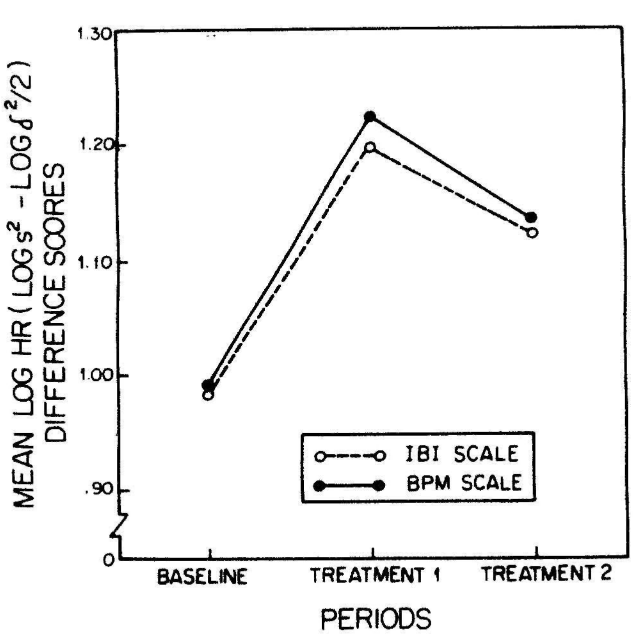

Fig. 2. Mean log s^2 minus log $\delta^2/2$ difference scores for baseline and treatment periods and for BPM and IBI scales.

As was noted in the introduction, in order to draw the conclusion that $\delta^2/2$ is empirically the preferable statistic, it must be demonstrated that linear trends differentially affect the periods being compared, and thus the value of s^2 for those periods. If the periods are not differentially affected, then s^2 will be similarly inflated for all periods and the conclusion regarding changes in HR variability would not be different from that obtained using $\delta^2/2$, though the estimate of σ^2 would be affected. In addition, to determine which combination of statistic and scale is most appropriate, it must be determined which scale is least affected by linear trends. The analysis of the results in Fig. 2 answer these questions. The Scale by Period interaction ($F(2/98)=26.27$, $MS_e=.00008$) showed that the BPM scale was significantly more affected by trends during the treatment periods than during the baseline period. The main effects were also significant and showed that the treatment periods had more systematic trends than the baseline period ($F(2/98)=13.59$, $MS_e=.094$), and the BPM scale was significantly more affected by trends than the IBI scale ($F(1/98)=65.51$, $MS_e=.0002$). A subsequent test of the means by the Tukey procedure (critical mean difference=.004) revealed that during the baseline and treatment periods, the BPM scale was significantly more affected by trends than the IBI scale.

The results of the above analysis show that nonrandom linear trends exist to a significant extent, but to different degrees depending on the observation period, in these HR data and seem to affect the BPM scale significantly more than the IBI scale. Therefore the appropriate HR variability analysis for the cognitive activity-cardiac variability hypothesis should involve the $\delta^2/2$ variability statistic, which is unaffected by linear trends and less affected by gradual trends than s^2, and the IBI scale, which seems to be less affected by linear trends than the BPM scale. Referring back to Fig. 1, it can be seen that when cognitive activity is increased using an arithmetic task, HR variability significantly decreases.

Discussion

The results of the present study demonstrate that contradictory conclusions regarding changes in HR variability can occur depending on the type of HR variability analysis conducted. It was shown that significant linear trends can exist in HR data and that these trends can have differential effects on the conditions being compared. Therefore, at least under the conditions of the present experiment, the s^2 statistic is an inappropriate statistic for measuring HR variability since: a) it is spuriously inflated by linear trends and thus overestimates the population parameter, and b) it is differentially inflated for each period being compared and thus confounds the results. The generality of this conclusion may be limited, however, to cases where small numbers of points contribute to the variability measure and in fact this reason may be a significant contributing factor to the finding of linear trends during the baseline period. The limitations on the generality of this conclusion are, however, questions for further empirical investigations. With this potential restriction in mind, it is nevertheless recommended that δ^2, or $\delta^2/2$, should be used as the statistic for measuring HR variability since it is unaffected by linear trends and minimizes the effects of gradual trends. Unless it can be demonstrated that differential linear trends do not exist in specific sets of HR data (e.g., comparisons between groups, periods, treatments, etc.), or that beat-by-beat cyclic trends do exist, the δ^2, or SDMS, statistic is recommended. Even minor, nonsignificant differences in the degree of linear trends between conditions could confound the results and conclusions to a significant extent, especially if the actual results are near the *a priori* set alpha level.

The results also revealed that, at least under the present conditions, the BPM scale is significantly more affected by linear trends than the IBI scale, and as trends increase during treatment, it affects the BPM scale increasingly more than the IBI scale so that the BPM scale becomes increasingly less valid as trend effects become more important. This result would suggest that the IBI scale is more appropriate for observing HR variability changes between different conditions than is the BPM scale. This conclusion adds some support to other investigations (Jennings et al., 1974; Khachaturian et al., 1972) which have suggested, on the basis of comparing moments of the BPM and IBI distributions, that the IBI scale is a preferable index of cardiac function to the BPM scale.

The results of this study also allow the speculation that the IBI scale should be used generally in preference to the BPM scale for detecting mean HR differences between conditions. Since the BPM scale is influenced by trends more than the IBI scale, the use of the IBI scale is recommended for increasing precision in HR experiments, which employ standard analysis of variance techniques to compare conditions, because the IBI scale should result in decreased variances for the conditions being compared. This designated preference for the IBI scale, however, is limited to those experiments where different conditions are being compared. In experiments where only one period is being considered, as where the concern is to observe changes in the topography of the HR response over time, the advantage of increased statistical precision of the IBI scale is probably eliminated since the relevent comparison in an analysis of variance is with a similarly inflated error variance within the same period. However, the validity of this speculation is still an open empirical issue.

Taken together, the results suggest that the SDMS-IBI combination is the most appropriate statistic and scale to observe and determine changes in HR variability, and the IBI scale may be generally preferable to the BPM scale for observing mean HR changes between conditions. From the point of view of the initial cognitive activity-cardiac variability hypothesis that predicts decreased variability during the treatment periods, this SDMS-IBI combination is also the best for detecting the predicted difference. The more usual technique using variance and the BPM scale would have resulted in an erroneous conclusion of no change in HR variability. These results add further support to those studies which have reported decreases in HR variability during attention-demanding tasks (e.g., Walter & Porges, 1976). However, the differences reported in those studies are difficult to assess since the effects of trends may alter the reported results, as might be observed if trend effects were reduced by using the SDMS statistic and IBI scale. It is likely, however, from the results of this study that the results reported by Walter and Porges (1976) may in fact be conservative due to the technique used to assess changes in HR variability. The present study, then, indicates that it is important to consider the effects of nonrandom trends in psychophysiological data where the variability of cardiac functioning is involved as the dependent measure of interest, and where it is suspected that differential changes in the degree of linear trend occur between the conditions being compared by traditional analysis of variance techniques.

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Announcements

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