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METHODOLOGY

Ambulatory monitoring of the impedance cardiogram

GONNEKE H. M. WILLEMSEN,[a] ECO J. C. DE GEUS,[a] COERT H. A. M. KLAVER,[a] LORENZ J. P. VAN DOORNEN,[a] AND DOUGLAS CARROLL[b]

[a]Department of Psychonomy, Vrije Universiteit, Amsterdam, The Netherlands
[b]School of Sport and Exercise Sciences, University of Birmingham, Birmingham, UK

Abstract

The growing need for more advanced ambulatory monitoring has led to the development of an ambulatory monitor for impedance cardiography (VU-AMD). This paper presents two studies addressing the validity of the VU-AMD. In the first study, the cardiovascular responses of 25 subjects during various conditions were simultaneously recorded with the VU-AMD and a standard laboratory impedance device. Correlations between the responses of the ambulatory and laboratory devices were high, both inter- and intraindividually, except for stroke volume and cardiac output during exercise. In the second study, 26 subjects underwent 24-hr monitoring with the VU-AMD. The values obtained with the VU-AMD were realistic and varied in a predictable way over activity and posture. It is concluded that the VU-AMD is a valid device for the measurement of systolic time intervals in real-life situations, but its applicability for absolute stroke volume and cardiac output determination remains to be established.

Descriptors: Ambulatory monitoring, Impedance cardiography, Systolic time intervals, Stroke volume, Cardiac output, Heart rate, Motility

The reactivity hypothesis regards hyperreactivity of the cardiovascular system to psychosocial stress as a stable individual characteristic that, when combined with exposure to chronic stress, increases the risk of developing cardiovascular disease, in particular, hypertension (Matthews et al., 1986). Most research directed at the reactivity hypothesis has concerned itself with laboratory stressors. However, in the laboratory, attention is almost always focused on acute cardiovascular functioning, applying short-lasting stressors with brief pretask and posttask periods, whereas the association between stress responses and cardiovascular disease might lie in the effects of exposure to more chronic stress or in the recovery and compensatory reactions during the day and night. More chronic changes of this sort cannot be investigated in the laboratory but require ambulatory monitoring.

For some time now, it has been possible to monitor heart rate, heart rate variability, and blood pressure in natural settings. Spectral analyses of ambulatory heart rate variability allows the identification of several frequency bands, including a high-frequency band and a low-frequency band, which are postulated to index parasympathetic–sympathetic interactions in cardiac functioning (Pagani et al., 1986). However, the low-frequency band has proved to be a very unreliable index of the sympathetic influence on the heart (Saul, Rea, Eckberg, Berger, & Cohen, 1990). It was, for instance, seen to decrease during steady state exercise, although the opposite would have been expected (Kamath, Fallen, & McKelvie, 1991). A major improvement in this regard would be the ambulatory monitoring of thoracic impedance to calculate the preejection period (PEP) and to estimate stroke volume (SV). The PEP has proved to be a reliable indicator of the sympathetic influence on the heart in pharmacological blockade studies and studies manipulating beta-adrenergic tone by exercise or emotional stress (Harris, Schoenfeld, & Weissler, 1967; Newlin, & Levenson, 1979; Sheps, Petrovick, Kizakevich, Wolfe, & Craige, 1982; Sherwood, Allen, Obrist, & Langer, 1986). PEP is an index of cardiac contractility (Newlin & Levenson, 1979), and changes in PEP during stress are considered to reflect predominantly beta-adrenergic effects of the heart (Sherwood et al., 1986). SV can be used to calculate cardiac output (CO), which in combination with ambulatory blood pressure monitoring, provides an estimate of the total peripheral resistance (Sherwood et al., 1990). These variables provide insight into the hemodynamic response pattern underlying blood pressure responses and might provide a more stable profile of reactivity than blood pressure responses alone (Sherwood & Turner, 1993).

Recently, an ambulatory monitoring device (VU-AMD) for thoracic impedance has been developed at the Department of Instrumentation of the Faculty of Psychology and Pedagogics of the Vrije Universiteit in Amsterdam. This paper reports two studies that examine the validity of this instrument for the measurement of interbeat interval (IBI), PEP, left-ventricular ejection time (LVET), SV, and CO. The first study examined the cross-instrument validity of the VU-AMD by comparing cardiovascu-

For information on the VU-AMD, please contact Eco J. C. de Geus, Faculteit Psychologie en Pedagogiek, Vrije Universiteit Amsterdam, De Boelelaan 1115, 1081 HV Amsterdam, The Netherlands.

Address reprint requests to: Gonneke Willemsen, School of Sport and Exercise Sciences, University of Birmingham, Birmingham B15 2TT, UK.

lar parameters simultaneously recorded by the VU-AMD and a standard laboratory impedance device. In the second study, 24-hr recordings with the VU-AMD were obtained, and changes in responses due to daily activity were investigated to determine the feasibility of ambulatory monitoring with the VU-AMD.

Study 1

To determine the cross-instrument validity of the VU-AMD, the electrocardiogram (ECG) and thoracic impedance were simultaneously recorded with the VU-AMD and a standard laboratory impedance device. Measurements were made under varying conditions of physical activity, posture, and psychological challenge to provide an indication of the performance of the VU-AMD.

Methods

Subjects. Twenty-five volunteer subjects, 11 men and 14 women, agreed to participate in the study. For the women, mean age was 25.4 years ($SD = 4.5$), mean height was 169.9 cm ($SD = 6.4$), and mean weight was 62.2 kg ($SD = 11.4$). For the men, mean age was 28.7 years ($SD = 12.3$), mean height was 183.6 cm ($SD = 11.2$), and mean weight was 75.2 kg ($SD = 6.2$).

Laboratory measurements: Signal recording and processing. The ECG and impedance cardiogram (ICG) were obtained from disposable pregelled Ag/AgCl electrodes (AMI type 1650-005 Medtronic). Measuring electrodes for the ECG were placed on the sternum over the first rib and between the eighth and ninth ribs just above the apex of the heart on the left lateral margin of the chest. An ECG ground electrode was placed on the abdomen above the right iliac crest. ECG was recorded with an amplifier with a time constant of 0.3 s and 1 MΩ input impedance. The thoracic impedance (Z), impedance change (dZ), and its first derative (dZ/dt) were recorded with the Nihon Kohden Impedance Plethysmograph (AI-601G) and Nihon Kohden Differentiator (ED-601G), using a tetrapolar spot electrode system (Zhang et al., 1986). The Nihon Kohden device yields a 350-mA constant current source with 50 kHz oscillator frequency. It has an electrode input impedance of 40 kΩ and output impedance of 40 kΩ. ICG current electrodes were placed on the back over cervical vertebra C4 and between thorax vertebras T8–T9. Measuring electrodes were placed at the base of the neck 4 cm above the jugular notch and over the sternum at the level of the fourth rib. The first derative of the impedance signal, dZ/dt, was recorded with a time constant of 5 ms by the Nihon Kohden Differentiator. The dZ/dt was passed to a 30-Hz high cutoff filter (6 dB roll off) of a Beckman Dynograph (R611) that was used for online display of the ECG and dZ/dt. Resulting signals were sampled continuously at 250 Hz by a 12-bit A/D converter and stored on 8-mm tape for later offline processing.

The ECG and ICG of each 1-min period were ensemble averaged with reference to the ECG R wave (Muzi et al., 1985). The averaged complexes of the ECG and ICG waves were used to compute the IBI, the R wave and B point interval (RBI), the PEP, the LVET, and the maximal rate of change of impedance (dZ/dt_{max}) according to the method described by de Geus, van Doornen, de Visser, and Orlebeke (1990). Briefly, IBI was defined as the time (ms) between successive R waves. RBI (in ms) was defined as the distance between the R wave and the B point. PEP (in ms) was defined as the time between the Q wave onset in the ECG and the B point in the dZ/dt signal. LVET (in ms) was defined as the time between the B and X points in the ICG. Detection of Q wave onset, B point, and X point was done automatically, but automatic scoring was always followed by interactive visual inspection of all ensemble averages. Automatic scoring of dZ/dt_{max} simply searched for the highest point in a 300-ms window after the R wave. The B point candidates had to lie within the interval between the R wave and the dZ/dt_{max}, and the X point had to lie in an interval of 500 ms after the dZ/dt_{max} and 512 ms after the R wave. To detect the B and X points, all zero crossings in either first or second derivative of dZ/dt in these windows were defined as possible candidates. "Bonus" points were assigned to these candidates based on preset criteria. For instance, the B point candidates received 3 points if they represented a zero crossing in first rather than second derivative, 2 points if they were the first candidate after the R wave, 3 points if the candidate's amplitude was near the $dZ/dt = 0$ line, 5 points if the candidate was followed by the positive slope with the greatest amplitude, 2 points if the candidate was within 20 ms of the location of the previous B point, and 2 points if the candidate yielded a PEP that fitted the equation PEP = 132 − 0.4 * heart rate (±15 ms) (Zoneraich, Zoneraich, & Rodenrys, 1974). During interactive visual scoring, the candidate with the most points was suggested by the program as the prime candidate for the B point.

To reduce respiratory artifacts, dZ/dt_{max} was defined as the difference between the maximal amplitude of dZ/dt and the amplitude of dZ/dt at the B point (Doerr, Miles, & Bassett Frey, 1981). Before each laboratory session, a 1-Ω/s calibration signal[1] was supplied to the measuring electrodes connected to the Nihon Kohden. The corresponding change in AD values was used to compute dZ/dt in ohms per second in later SV computations (the intrinsic calibration of the Nihon Kohden was not used, because it just tests the differentiator but bypasses the dZ measuring system).

SV was calculated using the formula proposed by Kubicek et al. (1974):

$$SV = \rho * (L0/Z0)^2 * LVET * dZ/dt_{max}$$

In this formula, ρ is the resistivity of the blood at 100 kHz, which is set to a constant value of 135 Ω/cm, because this has been shown to be as adequate as estimations using the hematocrit values (Quail, Traugott, Porges, & White, 1981; Traugott, Quail, & White, 1981). $L0$ is the distance between the ICG measuring electrodes and $Z0$ is the basic thoracic impedance signal read from the Nihon Kohden display at the end of each minute. Z0 calibration was done by means of 5 and 15 Ω resistors in a decade box (0.1% accuracy). Cardiac output was calculated as the product of heart rate and SV.

Ambulatory measurements: Signal recording and processing. The VU-AMD (32 × 65 × 120 mm and 225 g) can be worn un-

[1] The calibration signal is generated through the built-in digital/analogue converter (DAC) of a single-chip microprocessor (Hitachi H8532). This chip generates small sawtooth changes in the drain source voltage (Vds) of a field effect transistor (FET). A second identical FET is connected serially to get temperature stabilization. The FETs are connected parallel to a resistor determining Z0. After calibrating the circuit for 9.5 and 10.5 Ω with constant Vds for both resistances, this circuit yields a sawtooth signal of 1 Ω/s if the corresponding voltages Vds are applied as a sawtooth wave.

derneath clothing, is hardly visible to others, and allows subjects to follow their normal routines without having their movements constrained in any way.

The VU-AMD uses six disposable pregelled Ag/AgCl electrodes (AMI type 1650-005 Medtronic) to record both ECG and ICG signals (Figure 1). Electrode resistance (DC) is kept below 10 kΩ by cleaning with alcohol and rubbing. One electrode is a combined ECG/ICG electrode and is placed 4 cm above the jugular notch of the sternum. The other measuring ECG electrode is placed at the apex of the heart over the ninth rib, and a ground electrode is placed above the right iliac crest. The second ICG measuring electrode is placed directly over the tip of the xiphoid process of the sternum. This location is slightly below that of the recommended location over the fourth rib (Zhang et al., 1986). However, we found that using the xiphoid makes it easier to estimate simultaneously respiration from the *dZ* signal, which is an intended future use of the VU-AMD. Input impedance of the measuring system is 10 kΩ. The two current electrodes are placed on the back at the base of the neck (C3/C4) and over vertebras T8–T9.

Normally, the latter electrodes provide a 50-kHz, 350-mA current across the thorax. Because in this study ICG was also recorded with a static laboratory device (Nihon Kohden), the two currents across the thorax would cause interference. For this reason, the two current electrodes of the VU-AMD were not connected and the laboratory-derived current was used instead. Also, in this crossinstrument comparison study, three of the VU-AMD measuring electrodes could not be placed exactly on their normal locations, because these sites were already accommodating the measuring electrodes of the laboratory device. The two ECG and the upper ICG measuring electrode were placed 1.5 cm below and 1.5 cm to the right of the electrodes of the laboratory device. The lower VU-AMD ICG electrode was placed centrally over the xiphoid, which was well below the laboratory electrode.

In the VU-AMD, the ECG signal is relayed into a differential amplifier with 1 MΩ impedance and through a bandpass filter of 17 Hz ($Q = 33$). The R wave peak is recognized with a level detector with automatic level adjustment (Thakor, Webster, & Thompkins, 1983), and at each R wave peak a millisecond counter is read and reset to obtain the IBIs, which are stored continuously. The rest of the ECG signal is discarded. The impedance signal is amplified, relayed to a precision rectifier, and filtered at 750 Hz to obtain Z0. From Z0, *dZ* is obtained by continuously subtracting the integrated Z0 over the last 10 s. This procedure keeps *dZ* within amplifier range without producing discontinuities and is equivalent to the balancing circuit described by Hurwitz et al. (1993). The *dZ* is differentiated at 33.3 Hz to derive a *dZ/dt* that is subsequently passed through a 30-Hz high cutoff filter (12 dB/octave roll off). The resulting Z0, *dZ*, and *dZ/dt* are transmitted to the AD converter of the microprocessor. Z0 is sampled directly after the occurrence of each R wave. The *dZ* is sampled with a frequency of 10 Hz and *dZ/dt* is sampled at 250 Hz. The *dZ/dt* values are sampled only during a short period (512 ms) around each R wave and ensemble averaged over 60 s. All ensemble averages of the *dZ/dt* signal are stored in the VU-AMD, including the average Z0 from all beats in that minute period.

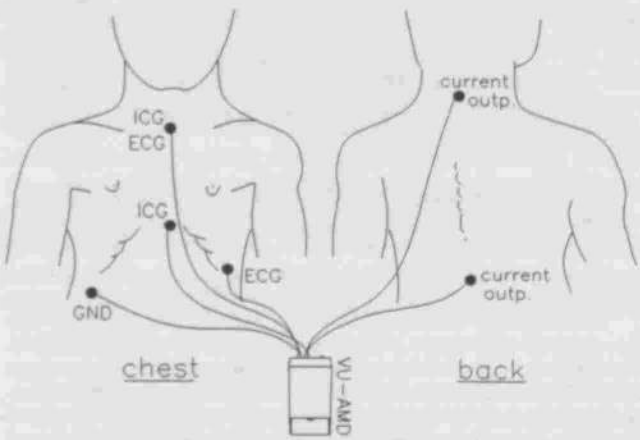

Figure 1. Placement of spot electrodes for registration of ECG and ICG when using the VU-AMD.

Before starting the recording, the VU-AMD was connected to an IBM-compatible PC by an interface suitable for the RS232 serial port. Dedicated VU-AMD software was used to set identification, time, date, and sample rates for the recorded variables. After recording, this software was used to read data from the VU-AMD and store it for later offline processing.

To compute IBI, RBI, PEP, LVET, SV, and CO, exactly the same algorithm was used as with the laboratory measurements, but because no average ECG complexes were stored, no Q wave onset could be determined. In the absence of the Q wave onset, we first determined the RBI as the distance between the R wave and the B point. Because PEP corresponds closely to isovolumetric contraction time, this abbreviated PEP may suffice as a measure of myocardial contractility. However, because PEP is the more known variable, we also estimated PEP by summing a fixed Q-to-R interval of 48 ms to this RBI.

Average noise amplitude in the *dZ/dt* was about 0.02 Ω/s, whereas average dZ/dt_{max} amplitude was around 0.9 Ω/s. In combination with R wave locked ensemble averaging this yielded clear *dZ/dt* complexes for all subjects across all conditions.

Procedure. Recordings with the VU-AMD and standard impedance device were simultaneously obtained during a 1-hr session. After an explanation of the procedure, subjects were placed in a soundproofed cabin, where the electrodes of the VU-AMD and standard laboratory instruments were connected. The protocol consisted of 11 conditions, starting with a 4-min period of relaxed sitting (RS1). Following this, subjects underwent 4 min of psychological stress testing, using the Tone Avoidance Reaction Time Task (TA), an active coping challenge. During this task, subjects were seated in front of a computer screen and were presented with a stimulus (an "X") that flashed briefly (500 ms) in one of the corners of the screen. They were instructed to respond as fast as possible to this stimulus by pressing the button opposite to this corner on the response panel. Incorrect or too slow responses were punished with a loud noise burst (1000 Hz, 85 dB), which lasted 500 ms. The task evokes both an increased cardiac adrenergic drive and an increase in vascular resistance (de Geus et al., 1990). On completion of this task, subjects returned to a 2-min period of relaxed sitting (RS2), after which they were asked to read an article aloud (RE) for 2 min. This was followed by a 2-min period of standing quietly (ST) and by a 2-min period of pacing up and down (WA), during which subjects walked across the cabin. After another 2-min period of relaxed sitting (RS3), subjects underwent paced breathing at 12 cycles per minute (cpm) (PB12) for 2 min, and then a 2-min period of paced breathing at 6 cpm (PB6). Dur-

ing the paced breathing conditions, subjects were seated and they were presented with a signal on a computer screen indicating when to inhale and exhale. This was followed by a 2-min period of relaxed sitting (RS4). The final condition was 7 min of bicycling (BC) at 50 W, which the subjects undertook seated upright on a bicycle ergometer placed outside the testing cabin. Only the last 4 min were used.

Data analysis. For each individual, the average IBI, RBI, PEP, LVET, SV, and CO values were computed for each period of the protocol, separately for the VU-AMD and standard impedance devices. Apart from the averaged levels, reactivity scores for all variables were computed for all active conditions (stress tasks, reading, standing, walking, paced breathing, and cycling) by subtracting the lowest value of the relaxed sitting periods. To avoid the problem of false positives, repeated-measures multivariate analyses of variance (MANOVAs) were performed to determine the condition effect and to determine whether either average levels or reactivity scores differed between the devices. For each condition, the correlations between the average values recorded with the VU-AMD and the standard device were also computed, as well as the correlations between reactivity scores obtained with both devices. Finally, for each individual, the crossinstrument correlation was determined across all separate minute values from all conditions to examine the variation across individuals in the extent of the association between VU-AMD and standard device measurements.

Results

The average values for IBI, RBI, PEP, LVET, SV, and CO for the two measurement devices during the various conditions are shown in Table 1. Significant condition effects were found for IBI ($F[10,15] = 27.98$, $p < .001$), RBI ($F[10,15] = 44.73$, $p < .001$), PEP ($F[10,15] = 44.24$, $p < .001$), LVET ($F[10,15] = 5.72$, $p < .001$), and CO ($F[10,15] = 4.41$, $p < .01$), but not for SV. Post hoc testing of the condition effect showed the expected effects of our manipulations on the cardiac time intervals. For instance, IBI, RBI, and PEP were seen to decrease during stress, walking, and bicycling in comparison with sitting at rest. Reading and paced breathing decreased LVET and IBI but did not affect RBI and PEP. In response to standing, IBI shortened, whereas RBI and PEP lengthened, probably reflecting a decrease in preload. Although SV was not significantly affected by the laboratory manipulations, the decrease in the IBI during walking and bicycling was mirrored by an increase in CO.

Our main question concerned the comparability of the two measurement methods. No significant instrument main effects or Instrument × Condition interactions were found for IBI, LVET, RBI, and PEP. Likewise, the VU-AMD and standard equipment did not differ in the registration of the reactivity scores of these cardiac time intervals. However, both SV ($F[1,24] = 2.73$, $p < .05$) and CO ($F[1,24] = 2.54$, $p = .05$) showed a significant Instrument × Condition interaction. Post hoc testing showed that the VU-AMD tended to overestimate SV and CO levels compared with the standard laboratory device in all conditions, but the difference was largest during standing and upright bicycling. In addition to the differences in the assessment of SV and CO levels, the two devices also differed in the assessment of SV and CO reactivity, computed as the change over resting baseline. Significant Condition × Instrument interactions for SV ($F[6,19] = 3.29$, $p < .05$) and CO ($F[6,18] = 2.96$, $p < .05$) reactivity arose mainly from a different response of the

Table 1. *Means and Standard Deviations of IBI, RBI, PEP, LVET, SV, and CO During Relaxed Sitting 1 (RS1), Tone Avoidance Task (TA), Relaxed Sitting 2 (RS2), Reading (RE), Standing (ST), Walking (WA), Relaxed Sitting 3 (RS3), Paced Breathing 12 bpm (PB12), Paced Breathing 6 bpm (PB6), Relaxed Sitting 4 (RS4), and Bicycling (BC)*

	Ambulatory IBI (ms)		Laboratory IBI (ms)		Ambulatory RBI (ms)		Laboratory RBI (ms)		Ambulatory PEP (ms)		Laboratory PEP (ms)		Ambulatory LVET (ms)		Laboratory LVET (ms)		Ambulatory SV (mL)		Laboratory SV (mL)		Ambulatory CO (L/min)		Laboratory CO (L/min)	
Condition	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
RS1	876.3	115.0	876.2	115.2	86.6	12.2	87.2	11.2	134.6	12.2	134.2	11.2	276.6	38.6	276.3	41.1	110.1	32.1	102.5	29.0	7.5	2.0	7.0	1.8
TA	824.4	124.0	824.1	124.2	81.4	14.6	82.0	13.9	129.4	14.6	129.4	13.4	276.0	40.6	275.4	43.1	102.1	32.8	97.1	29.5	7.5	2.7	7.1	2.4
RS2	886.2	118.4	884.6	118.3	85.7	14.2	85.7	13.4	133.7	14.2	132.7	13.6	280.1	40.7	280.3	41.1	110.0	32.8	104.0	30.7	7.5	2.3	7.1	2.1
RE	820.0	111.7	819.5	111.3	86.7	14.9	85.2	15.5	134.7	14.9	132.3	15.5	272.5	39.7	273.0	42.1	104.1	31.0	93.2	27.0	7.7	2.8	6.9	2.3
ST	772.3	128.5	772.4	129.8	95.3	10.0	93.6	8.9	143.3	10.0	141.1	9.8	258.0	36.4	259.4	36.6	98.3	33.2	89.4	27.4	7.4	1.7	6.8	1.4
WA	741.8	97.8	740.8	97.5	73.8	16.0	74.9	15.0	121.8	16.0	122.1	15.5	266.3	45.4	268.2	40.3	105.5	30.9	95.3	25.2	8.5	2.2	7.8	1.9
RS3	931.6	123.2	932.4	127.1	87.0	11.6	85.9	10.7	135.0	11.6	132.8	10.8	284.2	43.4	288.1	41.6	108.9	37.6	105.4	30.5	6.9	2.1	6.7	1.8
PB12	901.1	117.6	899.5	116.8	84.2	13.2	83.1	11.7	132.2	13.2	130.6	11.9	280.2	38.6	282.3	39.9	116.2	36.7	109.0	31.5	7.8	2.9	7.4	2.6
PB6	885.2	104.5	894.3	115.5	87.1	12.3	85.6	10.9	135.1	12.3	132.7	11.2	280.9	36.6	281.4	35.5	113.0	34.3	103.0	27.8	7.3	2.1	6.7	1.7
RS4	909.3	104.5	910.5	104.1	91.3	14.8	92.2	11.4	139.3	14.8	139.2	11.8	279.5	39.6	281.5	41.4	102.9	34.4	96.8	28.7	6.9	2.2	6.4	1.6
BC	606.4	91.0	605.8	90.7	47.0	16.7	47.0	18.3	95.0	16.7	93.5	18.6	257.4	23.6	259.2	22.6	119.1	30.9	81.0	46.8	12.1	3.7	8.4	5.3

two instruments to paced breathing at 12 cpm and bicycling. In both conditions, SV and CO reactivity was overestimated by the VU-AMD. SV and CO reactivity to the other conditions (stress, reading, standing, walking, and paced breathing at 6 cpm) did not differ with instrument.

Correlations between the average levels registered with the VU-AMD and standard laboratory device are presented in Table 2. They were very high for all variables across all conditions except for SV and CO during bicycling. Crossinstrument correlations for the reactivity scores are presented in Table 3. Although generally good agreement was found between the two instruments, only moderate correlations were found for RBI and PEP reactivity to paced breathing (12 cpm), standing, and bicycling. Again, clearly lower crossinstrument correspondence was found for SV and CO reactivity during exercise, although the correlations did reach significance.

To indicate the accuracy of the VU-AMD within individuals, correlations were determined between the two devices for IBI, RBI, PEP, LVET, SV, and CO during the entire experiment, that is, over all conditions. Because the previous results showed no correlation for SV and CO during bicycling and this could influence the intraindividual correlation, bicycling has not been included for these analyses (Table 4).

For IBI, intraindividual correlations are high, with only one case lower than .90 ($r = .67$, $p < .01$). For RBI and PEP, correlations were generally high (>.74), but moderate for four subjects (.48–.72), and no significant correlation was found in Subject 24. The correlations for PEP were generally as good as those for RBI, in spite of the fact that ambulatory PEP was estimated by summing a fixed interval of 48 ms to the RBI, whereas in the laboratory data, PEP was based on the true interval between Q wave onset and R wave peak interval (QRI) as scored from the combined ECG and ICG traces. This justifies the use of the estimated PEP in the VU-AMD. In fact, direct correlation of RBI and the true PEP in the laboratory data showed correlations varying between .87 (walking) and .98 (resting 2). Also, in the laboratory data, the average QRI across all conditions and subjects was 47.8, and very little variation was seen ($SD = 1.3$). For LVET, high intraindividual correlations were also found (>.72), except for modest but still significant coefficients for Subjects 11 and 24. In general, both SV and CO crossinstrument correspondence was good. Nonetheless, for SV, moderate coefficients (.52–.71) were found for five subjects, and for three subjects the coefficients were nonsignificant. Intraindividual correlations for CO were moderate for six subjects (.46–.71) and nonsignificant in Subjects 17 and 25.

Table 2. *Crossinstrument Correlation of Average Values in Each of the 11 Conditions (n = 25)*

Condition	IBI	RBI	PEP	LVET	SV	CO
RS1	1.00*	.95*	.92*	.99*	.79*	.76*
TA	1.00*	.94*	.92*	.99*	.79*	.84*
RS2	1.00*	.93*	.90*	.99*	.80*	.81*
RE	1.00*	.95*	.95*	.99*	.82*	.88*
ST	1.00*	.91*	.90*	.99*	.81*	.51*
WA	1.00*	.94*	.92*	.97*	.75*	.69*
RS3	1.00*	.88*	.85*	.99*	.77*	.73*
PB12	1.00*	.95*	.92*	.99*	.86*	.91*
PB6	1.00*	.92*	.87*	.99*	.84*	.84*
RS4	.98*	.86*	.85*	.98*	.80*	.73*
BC	.98*	.90*	.91*	.93*	−.03	.23

*$p < .01$.

Table 3. *Crossinstrument Correlations of the Reactivity Values*[a]

Condition	IBI	RBI	PEP	LVET	SV	CO
RE	.94*	.69*	.74*	.83*	.94*	.93*
PB12	.94*	.59*	.61*	.88*	.93*	.94*
PB6	.88*	.83*	.82*	.87*	.80*	.72*
TA	.95*	.83*	.83*	.81*	.92*	.92*
ST	.94*	.63*	.63*	.98*	.92*	.83*
WA	.95*	.82*	.83*	.73*	.73*	.77*
BC	1.00*	.62*	.63*	.95*	.54*	.55*

[a]Reactivity was computed with regard to the lowest resting value ($n = 25$).
*$p < .01$.

Study 2

To examine the feasibility of measuring with the VU-AMD in natural field settings, thoracic impedance and the ECG were monitored over a 24-hr period. The particular objectives of the study were to explore IBI, PEP, LVET, SV, and CO adjustments to various natural situations and to determine the influence of posture and activity on these parameters. In addition to the cardiac signals, subjects kept a diary of their activities throughout the 24 hr and motility was recorded.

Table 4. *Within-Subject Correlations Over 24-Min Averages Recorded in 10 Conditions*[a]

Subject	IBI	RBI	PEP	LVET	SV	CO
1	.99**	.98**	.98**	.81**	.94**	.97**
2	.94**	.85**	.85**	.91**	.70**	.84**
3	.99**	.94**	.95**	.82**	.95**	.85**
4	.99**	.70**	.68**	.98**	.97**	.98**
5	1.00**	.65**	.68**	.92**	.87**	.93**
6	.99**	.74**	.74**	.91**	.55**	.75**
7	.98**	.93**	.97**	.95**	.94**	.95**
8	1.00**	.79**	.79**	.93**	.94**	.81**
9	.99**	.80**	.80**	.83**	.99**	.98**
10	1.00**	.91**	.91**	.73**	.85**	.94**
11	1.00**	.80**	.82**	.53**	.29	.87**
12	1.00**	.94**	.94**	.92**	.97**	.90**
13	.99**	.59**	.48*	.93**	.52**	.71**
14	1.00**	.85**	.85**	.81**	.34	.50*
15	1.00**	.74**	.74**	.95**	.71**	.66**
16	1.00**	.75**	.75**	.96**	.86**	.47*
17	.96**	.80**	.80**	.89**	.66**	.40
18	1.00**	.92**	.92**	.95**	.85**	.77**
19	.99**	.82**	.82**	.86**	.91**	.91**
20	.98**	.79**	.72**	.81**	.89**	.90**
21	.99**	.93**	.92**	.88**	.98**	.96**
22	.99**	.66**	.71**	.90**	.88**	.86**
23	1.00**	.81**	.79**	.92**	.76**	.47*
24	.67**	.13	.13	.46*	.87**	.69**
25	1.00**	.77**	.69**	.80**	.00	.38

[a]The 4 min of bicycling were excluded.
*$p < .05$; **$p < .01$.

Methods

Subjects. Twenty-six male subjects with predominantly sedentary jobs took part in the study. Mean age was 44.8 (SD = 9.2), mean height was 183.1 cm (SD = 5.4), and mean weight was 79.8 kg (SD = 8.5). Subjects were paid Hfl. 50 for their participation. They were asked not to exercise during the ambulatory measurement or on the previous day.

Signal recording and processing. VU-AMD recording methodology was as described for Study 1 with one exception; in this study, the current across the thorax was now provided by electrodes from the VU-AMD. Also, to relate the physiological responses to the physical activity, the VU-AMD monitored the bodily movement of the subject. This motility (MOT) is measured as the vertical acceleration of the subject, which is an indicator of physical load (Montoye et al., 1983). The accelerometer consisted of an active acceleration sensor and its output was amplified, rectified, sampled, and reset every 5 s. The MOT values were determined by averaging these samples over periods of 30 s, and they have a range of 0–4 gs with a resolution of 0.008 gs. To secure the VU-AMD in a fixed position on the body, it was placed in a belt around the waist.

Data recording and processing was similar to Study 1, but the ICG and IBIs were not recorded continuously. The average IBI and MOT were stored every 30 s throughout the 24-hr recording period. In addition, a 5-min beat-to-beat recording (BBR) was automatically started by the VU-AMD every 20 min. During this BBR period, all IBIs were recorded and 1-min ensemble averages were computed for the dZ/dt signal. In addition, the average $Z0$ over these 1-min periods was stored. At the end of each 5-min period of detailed recording, the VU-AMD emitted an audible alarm to prompt the subject to fill out their activity diary. With this method, 15 out of each 20 min remained "unmonitored." Within the 5-min periods, however, there is a close link between physiological and behavioral data. As a corollary, the amount of ambulatory data becomes more manageable.

To ensure optimal quality of the incoming ECG and ICG signals, the beat-to-beat ICG signal was monitored online for 5 min at the start of each 24-hr session. The subjects were asked to breath deeply and to move about a bit. If signal quality was poor, the electrodes were refastened and/or new cables were used. In one case, the second measurement ICG electrode had to be moved below the level of the xiphoid to obtain a stable ICG signal. Because $L0$ is accounted for in the SV computation, we decided not to remove this subject.

At the start-up, the VU-AMD will start recording only if the incoming IBI times are constant within 12.5% of the average for eight consecutive R wave peaks. Once it has started, and throughout an entire ambulatory recording period, both the IBIs and the $Z0$ signal are constantly checked. If no new R wave arrives within 5 s after the previous R wave or if the $Z0$ leaves the 5–20 Ω range, data storage is suspended, whereupon the VU-AMD emits an audible signal. This feature is meant to prevent data loss by loose electrodes during ambulatory monitoring with the VU-AMD. When the subject refastens the electrodes, the device again looks for incoming IBIs constant within 12.5% of the average of eight consecutive R wave peaks. As soon as regularity of the incoming ECG is thus established and the $Z0$ is within the 5–20 Ω range, the VU-AMD silences its alarm signal and continues with data storage. The clock times of suspension and continuation of the data storage are always stored.

The activity diary invited subjects to describe the activities they had been engaged in during the last 20 min with emphasis on the final 5 min. In addition to the type of activity, they had to indicate their bodily posture (lying, sitting, standing, or walking), and to estimate their subjective stress level on a 4-point scale, ranging from none to severe. Following ambulatory recording, information from the diaries was combined with the heart rate and motility data using a graphical program. This program displayed heart rate and motility simultaneously with a time scale on the x axis, which made it possible to specify the start and end times of the activities more precisely. For instance, if a subject indicated that he walked to the canteen and sat down for a cup of coffee in the interval from 11:00 to 11:15, the graphical inspection of the motility and heart rate signals could be used to set the start and end of the walking (e.g., 11:02 to 11:06) and the start and end of the seated period (e.g., 11:06 to 11:18). All activities recorded in the diaries were classified with a text describing the type of activity plus a code for posture and movement. Because not all subjects undertook the same activities, various diary entries were grouped together in 15 main activity categories to facilitate comparison across subjects. These categories were sleeping, reading at home, watching television, social interaction at home (e.g., talking to spouse, playing with children, evening meal), general relaxation, drinking coffee/smoking, personal hygiene (e.g., dressing, cleaning teeth, washing), household activities (e.g., cooking, washing dishes), social interaction at work (e.g., meeting with colleagues, clients, or patients, telephone conversations), intellectual work (e.g., reading, word-processing, writing), walking, bicycling, traveling on public transport, car driving, and moderate physical activity (e.g., gardening).

Procedure. At the start of the 24-hr recording, subjects came to the laboratory where the experimenter showed them how to attach the VU-AMD and how to fill in the diary. In the event of the VU-AMD emitting an audible alarm, indicating a disturbance in the incoming ECG and ICG signals, subjects were instructed to check their electrodes and, when necessary, to reattach them. After attachment of the VU-AMD, the subjects left to follow their normal routines for 24 hr.

Results

None of the subjects reported discomfort from the device, not even during the night, and although 7 subjects had to reconnect the electrodes, this did not pose any problems. In 5 of the 26 subjects, substantial loss of data occurred due to equipment malfunction. No more than 50% of the recordings during the 24-hr cycle could be recovered. In three cases, loss of data was due to electrodes that became loose during the daytime and went undetected in spite of the alarm signal. In two cases, the cause of the malfunction was unknown. Very short interruptions of data recording (<1 min) were seen in virtually all subjects, which was due to loose electrodes. Apart from these recording problems, we found that no reliable scoring of the B or X points could be done in 17% of all ensemble-averaged ICG complexes. The identification of the B point, which indicates the onset of the left ventricular ejection, seems to be a pervasive problem in the analysis of impedance waveforms even in the laboratory (Sherwood et al., 1990). B point identification was even more difficult within field data, because there were more movement and breathing artifacts than is generally the case in laboratory settings. In addition to the B point, in some individuals detec-

Table 5. *Average Levels of Ambulatory IBI, PEP, LVET, SV, and CO as Recorded With the VU-AMD (N = 21)*[a]

	IBI (ms)		PEP (ms)		LVET (ms)		SV (mL)		CO (L/min)	
Activity	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Work (morning)	761.2	114.8	100.8	17.3	328.0	25.2	98.9	29.0	8.0	2.5
Work (afternoon)	744.0	93.4	96.6	17.3	324.9	29.6	101.5	34.2	8.3	2.6
Free time (evening)	811.8	93.0	103.4	17.5	341.1	21.3	104.7	32.1	7.9	2.6
Sleep (night)	961.4	103.4	122.8	14.2	361.6	24.4	108.1	28.1	6.9	2.0

[a]The average 24-h measurement period was subdivided in two work and two rest periods. Average duration of the periods was: work in the morning from 7:20 to 12:30, work in the afternoon from 13:00 to 17:50, leisure time in the evening from 17:50 to 23:10, and sleep from 23:30 to 6:55. The two work periods included driving to and from work.

tion of the X point, representing the closure of the aortic valve at the end of the left ventricular ejection, was difficult because of two or more waveforms in close proximity to the wave with the lowest *dZ/dt* point. The problems in identifying these points increased with the amount of movement.

In spite of data loss and scoring problems, a substantial data set remained. A total of 1,332 valid 5-min periods were available from a total of 21 subjects. These data were analyzed in three different ways, reflecting the various approaches that have been used in ambulatory research. First of all, we examined the average levels during the workday versus resting levels in the evening and during sleep.

Average IBI, PEP, LVET, SV, and CO were calculated over four intervals lasting approximately 5.0 hr each (Table 5). Repeated-measurement analysis (with MANOVA) showed a significant effect of time of day for IBI ($F[3,18] = 25.2$, $p < .001$) and PEP ($F[3,17] = 7.69$, $p < .001$). No difference was seen between the two work periods, but IBI and PEP were longer in the evening than at work. During sleep, significantly longer IBIs and PEPs were found than in the evening. No significant effects of time of day emerged for LVET, SV, and CO.

A second analysis was performed on the average levels during four different postures and walking. Five more subjects were excluded because data could not be obtained for all of the five conditions; this left an effective *N* of 16. Analysis of repeated measurements yielded significant posture/activity effects on IBI ($F[4,12] = 15,76$, $p < .001$), PEP ($F[4,12] = 11.75$, $p < .001$), LVET ($F[4,12] = 10.76$, $p < .001$), and CO ($F[4,12] = 3.26$, $p < .05$). Table 6 shows the expected decrease in IBI and LVET from supine to sitting to standing, with the lowest value found during walking. This was paralleled by a gradual decrease in PEP, although PEP did not discriminate between sitting quietly and sitting while moving or between standing and walking. Supine CO was significantly lower and CO during walking was significantly higher than CO in the other conditions. CO during sitting with and without movement did not differ from CO during standing. Table 6 also presents data on the 7 subjects that engaged in bicycling. Within-subject testing in these subjects over the six posture/activity conditions yielded significant effects for IBI ($F[5,2] = 45.1$, $p < .05$) and PEP ($F[5,2] = 60.8$, $p < .05$) and a trend for CO ($F[5,2] = 11.5$, $p = .082$). Post hoc contrasts revealed that during bicycling PEP and IBI were lower than during all other conditions, whereas CO clearly increased. Bicycling did not affect SV and LVET. However, because this group consisted of 7 subjects only, no direct comparison could be made with the averages of the other postures in the entire group of 16.

From Table 6 it is immediately clear that posture and physical activity are very important determinants of daily fluctuations in IBI, PEP, LVET, and CO. Generally, CO increased and PEP and IBI decreased with increasing physical activity level. This dependency was corroborated by the significant within-subject correlations of these parameters with motility. CO (.44–.66) and SV (.21–.56) were significantly higher if the subjects were active in all conditions, whereas IBI (−.52 to −.76), PEP (−.42 to −.82), and LVET (−.12 to −.47) decreased when motility was

Table 6. *Average Levels of Ambulatory IBI, PEP, LVET, SV, and CO as a Function of Posture and Physical Activity (N = 16)*[a]

	IBI (ms)		PEP (ms)		LVET (ms)		SV (mL)		CO (L/min)	
Posture	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Supine	979.3	120.8	124.0	15.1	367.7	23.2	105.3	31.4	6.6	2.2
Sitting[a]										
quietly	802.6	104.1	97.0	18.6	336.5	32.4	95.8	26.4	7.4	2.9
with occasional movement	761.3	102.4	97.6	15.3	321.9	47.7	100.5	22.8	8.1	2.1
Standing	741.3	125.4	92.6	17.5	326.1	26.4	100.8	36.8	8.4	3.6
Walking	723.5	120.2	91.6	11.2	310.9	36.4	110.7	31.6	9.6	3.2
Bicycling ($n = 7$)[b]	596.3	107.7	81.6	3.1	306.1	24.1	97.9	44.3	10.0	4.1

[a]Sitting was subdivided into quiet sitting with minimal movement (reading, listening, talking, watching TV, etc.) and sitting with occasional movement (car driving, repair work, writing, PC work). [b]Bicycling could be recorded in seven subjects only.

high. These correlations were all in the expected direction and point to the validity of the VU-AMD in a field situation at least in its sensitivity to physical activity and posture. As expected, there was no significant correlation between PEP and LVET. In addition, IBI showed the expected significant within-subject correlation with PEP (.32–.89) in 22 subjects and with CO (−.40 to −.44) in 21 of the subjects. Significant correlation between IBI and SV, however, was found in 5 subjects only.

Finally, a more detailed analysis was undertaken to determine the effects of specific activities. Because posture and physical activity had such clear effects on the ambulatory parameters, we decided to use data only from periods during which subjects were sitting or supine. Table 7 presents the average levels over the day for the three most-occurring leisure time activities and the three most-occurring work-related activities. For 14 of the subjects, at least 10 reliable 1-min ensemble averages could be obtained from these six categories. Significant effects of type of activity were found for IBI ($F[5,9] = 32.3$, $p < .001$) and PEP ($F[5,9] = 6.7$, $p < .01$). The effect for SV failed to reach the usual criterion of statistical significance ($F[5,9] = 2.4$, $p < .11$), although SV tended to be lower during intellectual work and television viewing. No effects across activities were found for LVET and CO. The absence of a significant effect for CO most likely reflected the large between-subject variation in CO.

Level during sleep was adopted as a baseline from which to compute reactivity to each of the 507 sedentary 5-min periods registered in Table 7, such as watching television, social interaction at home and at work, intellectual work, and car driving. At the end of each of these periods, subjects filled out their diaries, including an indication of subjective stressfulness of the activities they had engaged in. As expected, high stress ratings were associated with greater decreases in PEP (−.31 to −.46) and IBI (−.34 to −.51) in virtually all subjects. In addition, both SV (.09–.34) and CO (.23–.45) reactivity were significantly correlated with stress in 19 subjects.

Discussion

Ambulatory monitoring of cardiac impedance enables assessment of the hemodynamic basis of cardiovascular function in circumstances not accessible to standard laboratory impedance cardiography. Accordingly, its potential in cardiovascular stress research is considerable, particularly given the attention recently directed at the relationship between laboratory and field cardiovascular activity (Fahrenberg, Foerster, & Wilmers, 1993; Johnston et al., 1993; Pollak, 1991; van Egeren & Sparrow, 1989) and the significance of that relationship for the reactivity hypothesis (Pickering & Gerin, 1990; van Doornen & Turner, 1992). Study 1 revealed substantial correlations between systolic time intervals recorded with the VU-AMD and with a standard laboratory impedance device. Absolute values of PEP and LVET measured with both devices also showed good correspondence. Such high crossinstrument reliability is a necessary first step in establishing the validity of the VU-AMD for measuring levels of PEP and LVET in the field. However, absolute values of SV were overestimated with the VU-AMD in several conditions, and no significant crossinstrument correlation was observed for SV during bicycling. Sherwood et al. (1990) suggested that, at the level of the individual, absolute values of impedance-cardiography-derived SV may not be reliable. They advised the use of intraindividual changes in SV in repeated-measurements designs whenever possible. Accordingly, the reliable measurement of SV change or reactivity can be regarded as more critical than the reliable measurement of absolute SV values. In our study, crossinstrument comparison of SV reactivity was excellent in most conditions, although reactivity to walking and bicycling yielded only modestly high correlation coefficients (.54–.77). Because others have reported the reliable determination of SV during exercise from impedance cardiography using spot electrodes (Zhang et al., 1986), our difficulties would not appear to result from the use of spot electrodes per se. One possible explanation for the low crossinstrument correlation during exercise is the positioning of the second ICG measuring electrode over the xiphoid process, which is slightly lower than the recommended location over the fourth rib (Zhang et al., 1986). However, it is unclear why this should affect SV measurement with the VU-AMD only during exercise. A more likely explanation is the failure to detect correctly the X point in the ambulatory signal. In contrast to laboratory recording, no beat-to-beat editing facility was available for our ambulatory signal because only ensemble averages are stored. Single beats with severe waveform distortion, therefore, may have affected signal quality of the ambulatory impedance recording. Clearly, waveform distortions are more likely during exercise. In conclusion, the VU-AMD, as currently fabricated, does not measure SV reliably during moderate exertion. However, because most everyday psychological stressors are encountered seating or standing, poor performance during exercise may not be a major impediment.

The second study indicated the feasibility of spot electrode-based measurement of thoracic impedance in natural settings. Although far more data were lost in comparison with the laboratory, reliable ICG signals were recorded 81% of the time. The

Table 7. *Average Levels of Ambulatory IBI, PEP, LVET, SV, and CO as a Function of Activity (N = 14)*

	IBI (ms)		PEP (ms)		LVET (ms)		SV (mL)		CO (L/min)	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Sleeping	985.8	92.3	126.0	14.8	360.7	21.2	113.1	31.5	7.0	2.1
Watching television	839.3	83.1	107.2	8.9	335.5	31.4	91.2	20.1	6.6	1.5
Social interaction at home	765.5	99.4	102.6	20.9	324.9	41.7	106.3	24.4	8.3	1.9
Intellectual work	724.9	125.4	94.6	13.5	323.2	21.4	87.2	23.4	7.4	2.3
Social interaction at work	741.5	120.2	91.6	17.2	327.1	31.4	107.5	45.2	9.0	4.4
Car driving	779.0	100.2	99.7	19.0	321.3	44.1	104.9	34.2	8.4	3.6

Note: Only data from sitting or supine perods were used to obtain these average levels.

ICG yielded realistic values of PEP, LVET, SV, and CO in the field, which varied between extreme activities, such as sleeping and walking/bicycling, and across different postures. The responsiveness of PEP to psychosocial situations and its correlation with subjective stress suggests that ambulatory monitoring of stress-induced sympathetic reactivity is entirely feasible. Clearly, more studies using larger samples are needed to draw firm conclusions about the variation of systolic time intervals as a consequence of psychosocial stressors (e.g., those encountered at work). The clear dependence of our parameters on posture and motility poses a major problem for such an undertaking, because psychosocial effects must be disentangled from "mere" physical ones. To deal with this problem, we propose the use of an activity diary with frequent sampling. The strategy of the current study seems to be adequate. Every 20 min, the subjects were prompted to fill in the diary, with emphasis on the 5 min during which detailed physiological recording had taken place. Diary data were both verified and supplemented by the motility recording as in Study 2. Such recording clearly showed transitions in posture and activity such as standing up, sitting down, and walking.

In spite of the apparently plausible ambulatory levels of SV and CO found in this study, some major concerns remain about the validity of ambulatory SV measurements with the VU-AMD. First of all, we have to deal with a restriction that applies to all impedance cardiography-derived SV; namely, that the estimation is valid only in persons with structurally normal hearts (Sherwood et al, 1990). This seriously hampers the use of our instrument in a clinical setting. A second problem may be the use of spot electrodes instead of band electrodes. With regard to systolic time intervals, the spot electrode method yields results entirely comparable to the band electrode method (Boomsma, de Vries, & Orlebeke, 1989). This finding was replicated by Sherwood, Royal, Hutcheson, and Turner (1992) who, however, reported a fairly low correlation for CO values derived from band and spot electrodes (.47–.65). One could argue that these moderate correlations reflected the fact that spot and band electrodes were not tested simultaneously but one after the other. The latter introduces poor temporal stability of SV levels as a possible confounder of the spot versus band electrode comparison. In favor of spot electrodes, Zhang et al. (1986) showed that this method yielded SVs comparable to those estimated by CO_2 rebreathing. However, others have refuted these results (Patterson, Wang, McVeigh, Burns, & Cohn, 1993), and most of the invasive validation of the impedance-derived SV determination has been undertaken using band electrodes. The consensus seems to be that the spot electrode method still needs to be tested more rigorously (Sherwood et al., 1990). Third, some deterioration of SV estimation during high heart rate conditions may arise from the 30 Hz filtering of the *dZ/dt* signal (Hurwitz et al., 1993). Unfortunately, it is impossible to shield subjects from 50–60 Hz mains in field measurements, so at present high cutoff filtering is necessary. Finally, all validation of impedance cardiography-derived SV has been undertaken in laboratory set-ups. No experience exists with SV in natural field settings. In the ideal situation, our instrument would be validated against an invasive SV derivation method during a 24-hr field measurement. However, we know of no device capable of such invasive measurement. At best, therefore, the VU-AMD will be able to provide a crude estimate of 24-hr intraindividual changes in SV, and this only when posture is taken into account and physical activity is low. Given that no other noninvasive, nonobtrusive estimation of the ambulatory behavior of SV is available at present, this is not an inconsiderable achievement.

In conclusion, the VU-AMD seems to be a promising instrument in permitting the ambulatory measurement of thoracic impedance and the derivation of systolic time intervals and an estimation of SV and CO. The present data indicate that, in the laboratory, the VU-AMD, for the most part, performs as well as a standard impedance cardiograph, except for SV/CO estimation during conditions of exercise. In addition, it was shown that it is entirely feasible to use a device like the VU-AMD for recording the ICG in field situations, including registration during sleep. The pattern of results involving the PEP strongly suggests that valid estimation of changes in sympathetic nervous system activity is possible in natural settings. This new technology could yield important new insights into the link between chronic stress and disease.

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