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Assessing Autonomic Nervous System Activity

Wendy Berry Mendes

Changes in autonomic nervous system (ANS) activity can result from a variety of factors, including physical movement, postural changes, sleeping, disease, and aging. For social and personality psychologists, the value of examining the ANS may be that in many situations ANS responses can indicate shifts in emotion, motivation, attention, and preferences. Several obvious advantages of using ANS responses have been well established. For example, ANS responses are not susceptible to the self-report biases often engendered in sensitive contexts, in which individuals may be unwilling to report their unexpurgated feelings (Gardner, Gabriel, & Deikman, 2000; Guglielmi, 1999). In addition, obtaining data "online" allows for a dynamic analysis of moment-to-moment reactions that does not require introspective responses from participants. Other advantages are less obvious, however. ANS responses can temporally precede conscious awareness, revealing emotional responses or preferences that participants cannot yet report (Bechara, Damasio, Tranel, & Damasio, 1997). Finally, some patterns of ANS responding may be linked to mental and physical health vulnerabilities; these links may allow social and personality psychologists, along with clinical and health psychologists, to identify connections between social contexts or dispositions and disease etiology or progression.

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In this chapter, I first describe some of the primary techniques, for measuring ANS responses, together with methodological considerations and psychological inferences associated with each technique. Following these descriptions, I provide examples of some research programs that have effectively used the ANS to explore questions within social and personality psychology; I also speculate on some possible domains that have not been examined but may prove to be promising. In the third part, I describe some critical design features that are relevant when social and personality researchers are examining ANS responses. I conclude by describing future directions for the use of these types of measures in psychological research.

Primary Techniques for Measuring ANS Responses

The ANS is part of the peripheral nervous system, and primarily serves a regulatory function by helping the body adapt to internal and environmental demands, thereby maintaining homeostasis. Various measures can be used to assess changes in ANS activity. Here I review three broad, but related, categories—electrodermal activity; cardiovascular activity (e.g., heart rate variability, respiration, and cardiac output); and blood pressure responses—with a specific focus on measuring, scoring, editing, and interpreting these responses. In what follows, each measure is briefly described, and the general physiology of the measure is outlined; then measurement, scoring, and interpretative caveats are discussed.[1]

Electrodermal Activity

Electrodermal activity (EDA), also known by its outdated name "galvanic skin responses," is a fairly common measure of ANS activity and has a long history in psychological research. EDA measures responses in the eccrine sweat glands, which are found widely distributed across the body, but are densely distributed in the hands and soles of the feet. The sympathetic branch of the ANS system innervates these sweat glands, but a difference from most sympathetic responses is that the neurotransmitter involved in changes is acetylcholine rather than epinephrine.

EDA is commonly measured in one of two ways. The first method, skin conductance (SC), uses a small current passed through the skin

[1] Given the scope of this chapter, my descriptions of the underlying structure and function of the various systems are greatly oversimplified. References are provided to point the reader to reviews that are essential for a thorough understanding of the physiological responses reviewed here.

via a bipolar placement of sensors, and the resistance to that current is measured. The reciprocal of this resistance is SC. The second method, skin potential (SP), uses no external current and is collected with a unipolar placement of sensors. In addition to these methods of assessing EDA, there are two categories of data quantification that are based on how the EDA data are aggregated. When examining responses to a specific and identifiable stimulus, one looks at phasic activity, or the "response." When describing EDA that is not associated with a specific stimulus onset, but involves changes over longer periods of time (i.e., minutes rather than seconds), it is appropriate to examine tonic activity, or "level." Thus, with two methods of collection and two methods of quantifying changes, there are four categories of EDA data: SC response (SCR), SC level (SCL), SP response (SPR), and SP level (SPL). Choice of method and quantification should be determined by the specific questions under investigation, which are described in more detail below.

Preparation and Recording

To record SC, a bipolar placement of Ag/AgCl sensors are placed on the fingers, palms, or soles of the feet. If finger placement is used, it is recommended to put the sensors on adjacent fingers (second and third fingers, or fourth and fifth fingers), because they will be innervated by the same spinal nerve (Venables & Christie, 1973) (Figure 7.1). Unlike SC recording, SP recording requires a unipolar placement in which one electrode is placed on an active site (typically the palm of the hand) and the other sensor is placed on an inactive site (typically the forearm, though any inactive site would work).

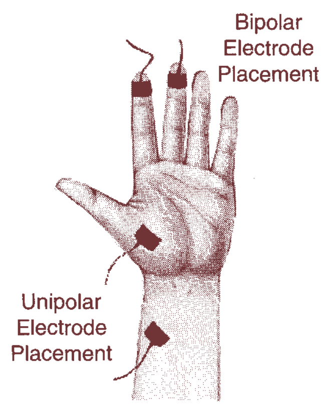


FIGURE 7.1. Placement of bipolar and unipolar leads for measurement of EDA.

Preparation of the skin should include a mild washing with water and a nonabrasive soap. Use of alcohol-based hand sanitizer or antibacterial soap prior to sensor placement is not recommended, because such products can excessively dry out the skin, resulting in lower levels of EDA and obscure sensitive changes. An electrolyte—either KCl, NaCl, or commercially available conductance cream—is then applied in a thin film on the two sensor sites, and also in the wells of the sensors. Once the sensors are attached, it is advised to wait several minutes (typically 5–15 min) before beginning the recording session. During this wait, one should check for sensor sensitivity. EDA responds to respiration, so the participant can be instructed to take a deep breath and hold the breath for a few seconds. A good EDA signal will show a change in response (an increase if SC is used, and a decrease if SP is used) within 2–3 sec once the breath is initiated.

Editing and Quantification

After data collection, waveforms should be inspected for movement artifact and electrical interference. Most scoring programs that are free or available for purchase will have options for editing waveforms that allow a coder to "spline," or interpolate, the area of the waveform that is affected by an artifact. This smoothing technique typically removes the influence of artifacts through interpolation by identifying the beginnings and ends of areas of the waveform that contain an artifact, and replacing them with estimates derived from adjacent areas.

When one is quantifying EDA to examine tonic levels (SCL or SPL), the decisions for averaging the waveform are time-based; that is, the waveform is averaged across a specified time period while a participant is at rest, and then over a similar time period when a participant is engaged in a task or activity. For example, reactivity values can be made in which 1 min of baseline data—typically the last minute or the minimum minute (when EDA reaches its nadir)—is subtracted from data quantified in 1-min intervals from a task. These new values then represent the change in EDA from resting to a task period. Alternatively, analysis of covariance or regression techniques can be used, in which baseline levels are added as covariates or repeated-measures analyses are used to examine changes over time.

A slightly more complicated approach related to quantification is required when one is examining responses linked to specific stimuli (SCR or SPR). In this case, an identifiable time-locked stimulus is presented to the participant, and a "trigger" or stimulus output is recorded online simultaneously with the EDA signal. A minimum threshold value of change needs to be determined so that a change in EDA can be identified as a "response" or not. Commonly, this threshold is set at 0.05

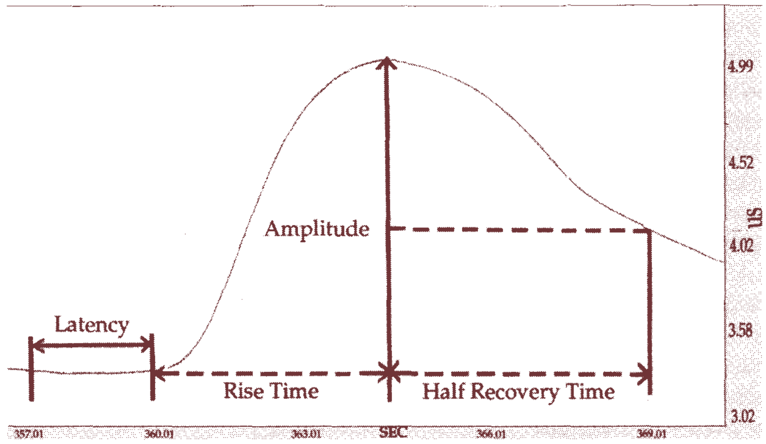


FIGURE 7.2. The SCR.

microsiemens (µS). Subsequent processing of data then allows for an estimate of the change in EDA linked to the specific stimulus. Several measures can be determined from this response: the latency from the stimulus to the initiation of rise time; the time from the initiation of rise time to the peak amplitude; the amplitude; and the time to reach "half-delta" (Figure 7.2). Half-delta is a time-based measure determined by examining the total magnitude of amplitude increase, dividing this by two, and then calculating the length of time from peak of amplitude to half of the magnitude of increase.

Levels versus Responses

The choice of collecting and scoring data based on either levels or responses should be dictated by the research questions and study design. For example, when experimental designs include presentations of specific stimuli in a time-locked, event-related design (e.g., affective pictures, pictures of members of different racial groups, etc.), it makes sense to score data as responses. When a study design includes events that unfold over time, and there are no specific time-locked events (e.g., social interactions, delivering speeches, nonscripted negotiations, etc.), then examining changes in EDA level from a baseline period to a task will be most appropriate. If the decision is made to examine changes in EDA level, one can still examine spontaneous responses, but the designation of these responses should be *nonspecific* SCRs. This measure is typically reported in number of nonspecific SCRs per minute, with resting or baseline averages ranging from 1 to 3 per minute. This measure can be used as a general index of anxiety or arousal resulting from some change in situational context, or linked to different dispositional factors.

Cardiovascular Measures

In simplest terms, the cardiovascular (CV) system consists of the heart and the pathways (vessels) through which oxygenated blood is delivered to the periphery of the body and deoxygenated blood returns to the heart. Psychologically, this system is responsive to affective states, motivation, attention, and reflexes. In addition, CV responses have been commonly linked to vulnerabilities in physical and mental illness. In this section, I review several methods that examine changes in the cardiac cycle: the electrocardiogram, measures of respiration, and impedance cardiography.

Electrocardiogram

The heart produces an electrical signal that can be measured with an electrocardiogram (ECG). A normal ECG recording is composed of various deflections referred to as P, Q, R, S, and T waves (Figure 7.3). Each heart cycle begins with an impulse from the sinoatrial node (not detected on the ECG wave), which results in a depolarization of the atria (P wave). The QRS complex represents the depolarization of the ventricles, and the T inflection indicates repolarization (or recovery) of the ventricles. These

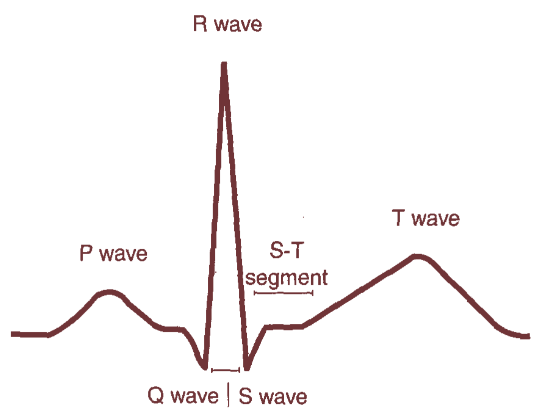


FIGURE 7.3. ECG waveform.

points in combination can be used to determine a variety of chronotropic (i.e., time-based) measures, such as the time of one complete heart cycle, known as the heart period (or interbeat interval). This measure is the inverse of heart rate (HR; beats per minute), though heart period is the preferred metric (see Berntson, Cacioppo, & Quigley, 1993).

PREPARATION AND RECORDING

ECG waveforms can be collected from several configurations of the limbs. Described below are three standard configurations in which placement results in an upward deflection of the Q-R complex:

Lead I: Electrodes are attached just above the right and left wrists on the inside of the arms. The left arm has the positively charged lead.

Lead II: Electrodes are attached on the right arm and left ankle. The ankle has the positively charged lead.

Lead III: Electrodes are attached on the left wrist and left ankle. The ankle has the positively charged lead.

Lead placements can be adjusted so that the sensors are placed on the torso rather than the limbs. For example, a modified Lead II configuration places the right lead below the sternum and the left lead on the left side of the torso below the ribcage. Torso placement may be deemed preferable over limb placement if there is anticipated movement of the limbs or if younger subjects (i.e., babies and toddlers) are being assessed.

Preparing the site for ECG placement can include gently abrading the skin and then applying a thin layer of conductance gel, but in many cases a clean signal can be obtained without any site preparation, given the strong electrical signal of the heart. Several factors that can interfere with an ECG recording should be anticipated, however. First, excessive hair on either the ankles or the chest can make recording difficult if adhesive disposable sensors are used. Shaving participants' ankles or chests may be possible, but could be problematic in some situations. Either adjusting the sensor location or using nonadhesive (i.e., band) electrodes may reduce the noise. Other potential problems include participants' skin type or changes in temperature during the course of the experiment. Skin that is especially oily or prone to sweat may require additional taping of disposable sensors, and even band electrodes may slip in extreme cases. Good lab practice includes taping the sensors with medical tape; this is especially true in summer months or for longer studies, when the risk of warmer skin temperature is greater.

EDITING AND QUANTIFICATION: ECG AND HRV

Editing an ECG waveform is typically done offline—that is, once the session is complete. The primary concerns in editing an ECG waveform are the proper identification of the R point and removal of artifacts that might appear to be an R point. Another critical point on the ECG waveform is the Q point, or the indication that the left ventricle is contracting. The Q point is critical for the calculation of the preejection period, which is considered to be one of the purest measures of sympathetic activation and is discussed below in the section on impedance cardiography.

Respiration can influence heart rate. For example, during inspiration, the influence of the vagus nerve on the heart is removed, and the HR accelerates; during expiration, the vagus nerve is applied, and HR decelerates. One way to examine cardiac changes from an ECG waveform, beyond HR/heart period, is to examine HR variability (HRV)—at its crudest level, $HR_{Max} - HR_{Min}$. HRV is influenced by a number of factors, but by deconstructing it one can isolate heart period changes due primarily to parasympathetic control, sympathetic control, or a combination of both. Of particular interest has been examining high-frequency HRV, because changes in variability in this range are believed to be due primarily to control of the vagus nerve and thus primarily indices of parasympathetic control. There are several measures of HRV estimates (time domain, frequency domain, and nonlinear measures), and a full committee report by the Society for Psychophysiological Research (SPR) is available for more details (Berntson, Bigger, & Eckberg, 1997). Here I briefly review some of the estimates and note what is needed to calculate these measures.

One of the simpler measures of HRV is based on time domain estimates—for example, root mean square of successive differences, which is calculated as the standard deviation of the beat-to-beat intervals. This measure is believed to reflect high-frequency HRV and respiratory sinus arrhythmia (RSA). A popular frequency domain technique to estimate HRV involves decomposing heart period variance into different frequency bands by using Fourier transformation. For example, the high-frequency band ranges from 0.15 to 0.4 Hz (cycles per second); it is thought to represent primarily vagal influence and, as such, parasympathetic activity. Lower-frequency bands (<0.15) have also been identified, and in these frequency domains the influence can be either sympathetic or parasympathetic.

Note that in the examples above, respiration rate is not factored into the analyses; instead, rate of breathing is assumed rather than measured. One commonly debated measurement issue in HRV research concerns the importance of controlling for respiration rate and depth in HRV analysis. For a thorough understanding of the complexities of this issue, see Denver, Reed, and Porges (2007) for justification that respiration frequency need not be included in estimates of RSA/HRV, and Grossman and Taylor (2007) for a discussion of why respiration frequencies are important.

Measures of Respiration

Respiration can be measured in a number of ways. One option is to use a strain gauge that measures pressure during inspiration and expiration, and rate and depth of breaths can be extracted. If a single strain gauge is used, the recommended placement is high on the torso immediately under the arms (and above the breasts). This placement will allow for measurement of upper respiration, but not lower abdominal respiration, which may be important if the research focuses on the type of deep breathing found in meditation or other focused breathing domains. In this case, two strain gauges can be used to provide both upper and lower respiration. Another option is to use impedance cardiography, which can extract respiration rate and amplitude.

Impedance Cardiography

Impedance cardiography is a noninvasive technique to estimate blood flow changes in the heart. This technique allows for estimates of how much blood is ejected during each heart cycle (stroke volume, or SV), and various changes in the cardiac cycle (e.g., the timing of the aortic valve's opening and closing). In combination with an ECG signal and blood pressure responses, a variety of cardiovascular changes can be assessed or derived.

Impedance cardiography requires the use of either spot or band electrodes[2] placed on the torso (Figure 7.4). Using an output of electrical current (ranging from 1 to 4 mA) to the two outer sensors, the inner sensors detect the resistance to the incoming current. This resistance to the current (or impedance) presents global blood flow in the thoracic cavity (typically referred to as Z_0, or basal impedance). As the blood volume increases, the impedance decreases. The first derivative of the

[2]The use of band versus spot electrodes is a topic of ongoing debate among psychophysiologists. For experimenter ease and participant comfort, spot electrodes may be preferable and appear to estimate SV reliably while subjects are at rest. However, band electrodes appear to more accurately reflect changes in cardiac output during stress/challenge conditions, because of detection of changes in the thoracic cavity that may be missed by spot electrodes (see Brownley, Hurwitz, & Schneiderman, 2000).

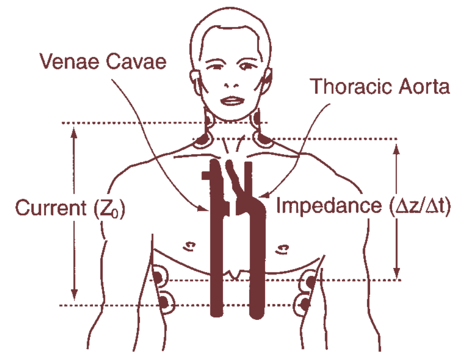


FIGURE 7.4. Impedance cardiography and placement of band sensors.

waveform—Δz/Δt, or the change in basal impedance over the change in time—provides a measure of the blood volume ejected from the heart on each beat.

As Figure 7.5 shows, the Δz/Δt has several critical inflection and deflection points that are identified either with a software program or manually. Several of these points are critical to the identification of responses occurring in the cardiac cycle. For example, a chronotropic measure of ventricle contractile force is the preejection period (PEP). This is the time from the left ventricle contracting (Q point on the ECG wave) to the aortic valve opening (B point on the Δz/Δt waveform). SV, the amount of blood ejected from the heart on any given cardiac cycle, is a measure that requires the identification of the B point and X point on the Δz/Δt waveform to determine the time when blood is being emptied at the aorta, along with the maximum point of the Δz/Δt waveform on the given cardiac cycle labeled Z[3] in Figure 7.5.

SV provides an estimate of the amount of blood ejected at each beat; however, in terms of an overall indication of how much blood is being pumped through the heart in any given minute, cardiac output (CO) is the preferred measure. CO is simply the product of SV and HR (SV × HR/1000). SV is reported in milliliters, so the product is divided by 1000 to report CO in liters per minute. Because CO is a combination of both heart speed and blood volume processed in the heart, it is believed to be a measure of cardiac efficiency.

When impedance cardiography is being used in a laboratory setting, it is important to tell participants to wear comfortable, two-piece cloth-

[3] The Z point is sometimes identified as the C point.

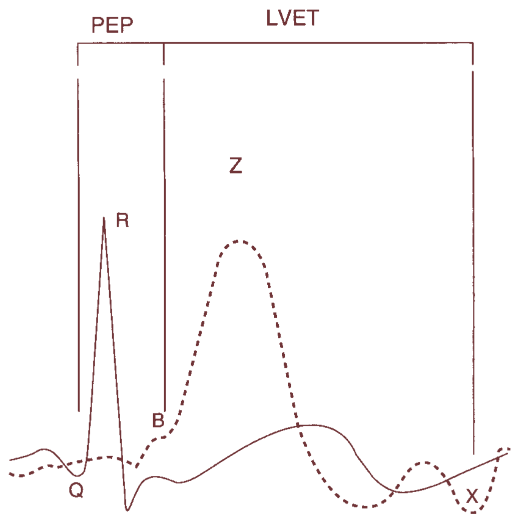


FIGURE 7.5. Dz/Dt and ECG waveforms needed to score PEP, LVET, and SV.

ing to the experiment. As the bands (or spots) require placement on the torso, directly on the skin, participants are required to lift their shirts to expose their torsos. In addition, placement of the neck sensors may be impeded by clothing that is snug on the neck. In my lab, we keep extra shirts and pants for participants who arrive in clothing that would make attachment of the bands difficult.

EDITING AND QUANTIFICATION

Probably among the greatest challenges for researchers interested in impedance cardiography are editing and summarizing the data. First, there are some important choices to be made regarding how the data are summarized for editing. One option uses ensembled waveform averages. This method determines the composite or average waveform across some specified time period (typically between 30 sec and 5 min). When the waveforms are "averaged" over time, random noise and movement are removed, and a more representative cardiac cycle can be obtained. Another option is to determine blood volume changes on a cycle-to-cycle basis (see an SPR committee guideline paper by Sherwood et al., 1990).

In addition to how the data are averaged, there are several different formulas that can be used to estimate SV. The Kubicek equation estimates SV from the derivative of the impedance signal and blood resistivity:

$$SV = \rho \times L2 / Z_0^2 \times \Delta Z/\Delta t_{max} \times LVET$$

where $\rho = 135$ (blood resistivity), L is the distance between electrodes, $\Delta Z/\Delta t_{max}$ is the peak amplitude of $\Delta Z/\Delta t$, and LVET is the left ventricle ejection time (time in milliseconds between B and X).

More recently, other equations have been offered that may be superior to Kubicek's. For example, the Sramek–Bernstein equation estimates SV from the volume of electrically participating tissue (VEPT), scaled according to body surface:

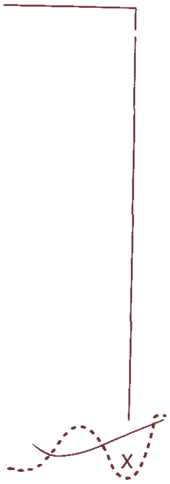
$$SV = \delta\,(VEPT) / Z_0 \times \Delta Z/\Delta t_{max} \times LVET$$

where $\delta\,(VEPT) = weight_{max} / weight_{ideal} \times (0.17H)^3 / 4.25$ (participant's height, weight, and ideal weight are needed).

Regardless of the equation used, one of the most critical decisions in scoring impedance data is accurately identifying the B point on the $\Delta z/\Delta t$ waveform. Though it is tremendously time- and labor-intensive, the technique that assures the greatest accuracy is manual detection of the B point. Specifically B should be placed at the beginning of the longest uphill slope before the Z point (Figure 7.5). Algorithms have been developed to assist in detecting the B point, such as placing the B point at 56% of the distance between Q and Z (see Berntson, Quigley, & Lozano, 2007), but in our own examination of this method, we have found that from 20% to 40% of the time the program does not mark the B point where we can visually confirm it (Mendes & Koslov, 2008). Importantly, the variability in accuracy changes, depending on whether the data are from a baseline period (where accuracy tends to be higher) or whether the participants are engaged in a stressful task (e.g., mental arithmetic in the presence of stoic evaluators).

Blood Pressure

Blood pressure (BP), measured in millimeters of mercury pressure (mm Hg), refers to the amount of pressure on the vessel walls during the cardiac cycle. Distinctions are made between systolic BP (SBP) and diastolic BP (DBP), which represent peak pressure and lowest pressure in the arteries, respectively. Though correlated, these measures may provide unique information and are thus typically both presented. For example, during stressful or emotionally provocative situations, increases in SBP



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Although SBP and DBP are often presented separately, one will also find instances in which researchers combine the two in some meaningful way. For example, pulse pressure (PP) is calculated by subtracting DBP from SBP (PP = SBP – DBP). At rest, average PP is approximately 40 mm Hg. During exercise, SBP typically increases more than DBP. Extremes in PP in both directions can indicate abnormalities. When PP is too high, this is likely due to artery stiffness, leaky aortic valves, or hyperthyroidism and has been linked to CV complications (Blacher et al., 2000). Low PP values, typically influenced by low SV, can indicate abnormalities such as congestive heart failure.

Another type of averaging is mean arterial pressure (MAP), which is calculated as a type of average (though not an exact mathematical average, because DBP is weighted more, given its longer time course within a given cardiac cycle): $MAP \approx [(2 \times DBP) + SBP]/3$. MAP is often used in combination with CO to determine total peripheral resistance (TPR), according to this formula: $TPR = (MAP/CO) \times 80$. Changes in TPR can be construed as an estimate of the amount of constriction versus dilation occurring in the blood vessels—specifically, the arterioles. When the arterioles constrict, less blood can flow to the periphery, and this is indicated by an increase in TPR. In contrast, when arterioles expand, or vasodilate, this allows more blood flow and is indicated by decreases in TPR.

BP can be obtained from various places on the body, including the brachial artery (upper arm), the radial artery (wrist), or the finger. It is important to point out, however, that as the distance from the heart is increased, the accuracy of BP changes is reduced. BP measurements can be obtained via several techniques. One option is the auscultatory method, which consists of temporally stopping blood flow at the brachial artery and listening for Kortokoff sounds indicating blood flow in the arteries—the pressure when blood first begins to flow is SBP, and the pressure when blood flow sounds stop is DBP. A trained professional using this technique employs a sphygmomanometer and stethoscope to obtain BP.

However, in many cases psychologists want to obtain BP in a less labor-intensive way, and/or one that minimizes the self-consciousness that may arise from having BP measured. Digital BP machines are rela-

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tively inexpensive and fairly accurate measures of BP levels (though not as precise as a trained professional using a sphygmomanometer). Again, these BP machines typically require occluding the brachial artery every time a BP measurement is desired. This is not difficult, but could potentially distract participants from the experimental situation. A potential solution for obtaining BP responses over time, which is only minimally invasive, is with a continual or continuous BP monitor. *Continual* monitors are so designated because BP responses are estimated over some given number of cardiac cycles (e.g., BP over 15 cardiac cycles). *Continuous* BP machines have the additional advantage of obtaining BP responses on every cardiac cycle. Commercially available machines are manufactured by Colin Medical Instruments (San Antonio, TX) and Mindware Technologies (Gahanna, OH).

Many continual or continuous BP machines use either oscillometric or tonometric technology. Oscillometric technology initially inflates a cuff over the brachial artery, deflates until the point at which SBP can be measured, and then keeps a constant cuff pressure. The technology and algorithms used for these machines are proprietary, so there is some concern about comparing results across laboratories. Tonometric technology consists of BP measurement from the radial (wrist) artery, and uses a sweep technique, which applies a varying force on the artery. This technology can be very sensitive to movement and sensor positioning relative to the heart. Manufacturers recommend putting the arm in a sling so as to position the sensor at heart height and limit movement. For social and personality psychologists, who often aim for strong ecological validity, restraining the arm can be problematic. However, my lab's own use of this technology suggests that movement is the greater problem. Fashioning a cradle that will keep the arm and wrist stable throughout the experiment is imperative to obtaining good measurements. Some of the more expensive machines include an additional brachial cuff BP device to allow for online comparisons from the two sites; the wrist cuff can be signaled to reposition if the brachial BP responses differ from BP measured at the radial artery.

ANS Responses in Social and Personality Psychology

Social and personality research using ANS responses is plentiful. Here I review some selected studies; this review is not meant to be exhaustive and is influenced by my own research interests in emotion, stress, motivation, attitudes, and intergroup relations. For ease, I have based the organization of sections on the physiological measurements used rather than the psychological constructs under examination.

Electrodermal Responses

As previously described, changes in EDA can index general arousal; thus the use of these measures may at first seem limited. However, both classic and contemporary uses of these measures show that compelling information can be obtained by looking at EDA. Indeed, using peripheral measures in the domains of emotion, motivation, and attention has provided important empirical evidence for social and personality psychologists.

For example, SC has been used in the context of emotional disclosure. Pennebaker, Hughes, and O'Heeron (1987) examined changes in SCL while participants disclosed traumatic events from their lives. Talking about traumatic events decreased SCL in participants classified as high disclosers, relative to those classified as low disclosers. This finding has been used as a possible explanation of why there are physical and mental health benefits of confession: High disclosers showed lower sympathetic activation than low disclosers.

Whereas getting something traumatic off one's chest may be beneficial, forcing oneself to feel good may be detrimental. Wegner, Broome, and Blumberg (1997) instructed participants either to relax or not to relax while answering questions that were believed to index intelligence (a high-cognitive-load condition) or answering the same questions that were described as test items (a low-cognitive-load condition). For participants in the high-cognitive-load condition, the instruction to relax resulted in higher SCL than did the instruction not to relax. These findings nicely demonstrate the potentially ironic effects of *trying* to relax, which resulted in greater sympathetic activation.

Not surprisingly, ANS responses in general, and EDA measures in particular, are often used in research examining gender biases and race relations because of the difficulty in obtaining unexpurgated self-reported responses. In a recent study, changes in SCL were used to examine threatening gender environments, involving an imbalance of males to females (Murphy, Steele, & Gross, 2007). In this research, male and female participants viewed one of two videos that presented either a gender-balanced group of students or a gender-unbalanced group (mostly white males) in the domain of a math and engineering science camp. Changes in SCL from a baseline period to watching the videos were computed. The findings were that female participants showed greater increases in SCL when watching the gender-unbalanced video than watching the gender-balanced video, and male participants did not differ in their SCL responses as a function of the videos' gender composition. The authors concluded that the gender imbalance was especially threatening for women.

can index general arousal seem limited. However, both easures show that compelling r EDA. Indeed, using periph- motivation, and attention has r social and personality psy-

context of emotional disclo- 1987) examined changes in events from their lives. Talk- in participants classified as s low disclosers. This finding why there are physical and disclosers showed lower sym-

off one's chest may be benefi- rimental. Wegner, Broome, es either to relax or not to believed to index intelligence g the same questions that e-load condition). For par- the instruction to relax not to relax. These find- effects of *trying* to relax, on.

eral, and EDA measures mining gender biases and ining unexpurgated self- es in SCL were used to involving an imbalance of . In this research, male ideos that presented either gender-unbalanced group and engineering science to watching the videos male participants showed gender-unbalanced video male participants did not the videos' gender compo- balance was especially

In these examples, EDA was used as a general measure of arousal or anxiety. However, by limiting the context, one can increase the inference of EDA changes. For example, in fear conditioning paradigms, an electric shock or other aversive stimulus is paired with some unconditioned stimulus while SCRs are measured. In learning phases, the shock or other aversive stimulus is repeatedly linked in time with the conditioned stimulus. Later the shock is removed and SCRs are examined upon exposure to the conditioned stimulus. The critical examination is the length of the extinction phase, or how long it takes for participants to cease showing SCRs to the conditioned stimulus once the aversive element is removed. An exceptionally creative adaptation of this design has been described in a *Science* article by Olsson, Ebert, Banaji, and Phelps (2005). In this study, the researchers paired electric shock with ingroup and outgroup male faces. They argued that individuals might be evolutionarily "prepared" to fear outgroup members and, because of this, that extinction of the fear response would take longer when the shock was paired with outgroup faces than when it was paired with ingroup faces. Indeed, when shocks were paired with outgroup faces compared to ingroup faces, SCRs persisted longer and were of greater magnitude in the extinction phase. In this example, SCRs could be interpreted as fear responses because the context was constrained to a fear-eliciting (shock) situation.

SC changes may index emotional responses even prior to the conscious awareness of those emotions. An elegant example of the possibility that physiology may provide information regarding emotional and motivational responses before conscious awareness is provided by Bechara and colleagues (1997). These investigators measured SC changes while participants (individuals with and without prefrontal brain damage) learned decision rules for a card task. Although self-reported indications related to "hunches" regarding decks that were associated with more gain than loss cards developed by the 50th trial for the control participants (i.e., those without brain damage), SC changes in anticipation to the loss decks occurred typically by the 10th trial, which preceded conscious awareness by approximately 40 trials. That is, SCRs suggested an intuition of an impending loss prior to the nondisabled participants' conscious awareness of the intuitions they were developing.

Heart Rate Variability

Of growing interest to social and personality psychologists are measures capitalizing on the variability of the cardiac cycle. Initially, HRV was believed to be a measurement artifact or nuisance, but further exploration into spontaneous changes in the timing of the heart cycle proved to be psychologically and physiologically meaningful. Though there are still disagreements on the specifics related to measurement, quantification, and psychological meaningfulness of vagal tone and cardiac vagal reactivity (see Chambers & Allen, 2007), these measures may prove to be especially important for social and personality psychologists interested in emotion and/or mental effort.

Though most work has focused on resting/baseline RSA (also known as cardiac vagal tone) and its links to dispositions and responses to social and emotional situations, there is also a growing literature on vagal reactivity and vagal rebound. Vagal rebound is the extent to which RSA responses return to or even overshoot baseline levels after some suppression of the vagal brake. Below I review some literature exploring these various components of HRV.

One theory that has received much attention in terms of the inferences one can draw from HRV is Porges's polyvagal theory (e.g., Porges, 2007). Porges (2007) argues that vagal regulation stemming from the nucleus ambiguus and enervation from cranial nerve X acts on the vagus nerve to modulate heart period. The polyvagal theory further specifies that primates uniquely have vagal nerve modulation (but see Grossman & Taylor, 2007), which has evolved as part of the social engagement system. One of the primary postulates of polyvagal theory is that social factors (affiliation, social engagement) or personality factors (bonding, compassion) can modulate vagal activity. Specifically, Porges argues that higher RSA (higher cardiac vagal tone) can be used as an index of adaptive emotional regulation and responsiveness to the social environment. Similarly, cardiac vagal reactivity may also index appropriate social engagement, in that increased vagal reactivity during a task may be associated with calmness, equanimity, and a lack of distress.

Adding some complexity to these effects, however, is the nature of the social context. In highly stressful situations or tasks that require some amount of mental attention or effort, then one should expect a withdrawal of the vagal brake (resulting in lower RSA) to indicate greater attentional control and effort. Indeed, cognitive psychophysiologists have used decreased RSA as an index of attention or mental effort (Tattersall & Hockey, 1995). In one study relying on this type of interpretation for HRV reactivity, Croizet, Després, and Gauzins (2004) examined changes in RSA during a stereotype threat paradigm. They found that participants assigned to receive a stereotype threat prime had a greater decrease in RSA and poorer performance than those in the control condition, and that RSA changes mediated the relationship from the condition to the performance effects.

Applications of cardiac vagal tone and vagal reactivity are increasing in personality and social psychology. Some applications have focused on the extent to which dispositional emotional styles are linked with cardiac vagal tone (Demaree & Everhart, 2004; Sloan, Bagiella, & Shapiro, 2001). For example, do individuals with greater hostile tendencies have lower cardiac vagal tone? In an examination of this question, researchers found that those higher in hostility tended to have lower cardiac vagal tone at baseline, during an emotional induction task, and at recovery than those lower in hostile tendencies did (Sloan et al., 2001; cf. Demaree & Everhart, 2004).

Recently, RSA has been examined as a possible mediator for why implicit goal setting may result in improved performance. In a previous study, participants who exaggerated reports of their grade point average (GPA) tended to improve their GPA more than those who did not exaggerate (Gramzow & Willard, 2006). Was exaggeration a form of implicit goal setting or simply a form of anxious repression? We examined RSA reactivity as a way to differentiate anxious orientation while exaggerating from motivated goal setting (Gramzow, Willard, & Mendes, 2008). In this study, participants first reported their GPA and course grades in private, and then met with an experimenter to review their academic history. During this interview, the participant's ECG and respiration were recorded, and RSA responses were then calculated. We found that the more participants exaggerated their GPA, the greater the increase in RSA from baseline to the interview, suggesting that participants who exaggerated their GPA were not necessarily anxious about their exaggerated standards. In addition, those who had greater increases in RSA when discussing their GPA tended to improve their GPA in a subsequent semester. Converging evidence from nonverbal behavior coded during the interview suggested that exaggerators appeared composed rather than anxious, supporting the interpretation that higher RSA while discussing one's GPA was associated with equanimity rather than anxiety.

Impedance Cardiography

CV responses have been used extensively in the areas of motivation, emotion, and stress. Interest in these measures is further fueled by the possibility that certain patterns or response profiles of CV responses repeatedly experienced over time may be linked to health outcomes. Early work *linking Type A personality and coronary heart disease examined CV* responses as one of the likely mechanisms through which physical health was affected. Specifically, it was theorized that excessive CV responses would create tears in the endothelial lining, resulting in greater calcifications and plaque buildup that could possibly initiate ischemic events or strokes. Primarily, CV responses in this context included HR (heart period) and BP responses.

A combination of CV and BP responses is used in research attempting to index challenge and threat states. Though not without its critics (Wright & Kirby, 2003; see also Blascovich, Mendes, Tomaka, Salomon, & Seery, 2003), this line of research attempts to differentiate motivational states by using various CV measures, such as PEP, CO, and TPR. The theory behind this research argues that in motivated performance situations (i.e., those that are active rather than passive and require some cognitive or behavioral responses), CV responses produce a distinct profile of reactions that can differentiate motivational states related to approach/activation from those related to defeat/inhibition (Mendes, Major, McCoy, & Blascovich, 2008). Early work on this theory showed that task appraisals that showed greater resources relative to demands were associated with greater CV responses: shorter PEP (indicating greater ventricle contractility), increased HR and CO, and decreases in vascular resistance (lower TPR). This pattern of CV reactivity was believed to be a marker of psychological states of challenge. In contrast, appraisals that showed greater perceived demands relative to resources to cope were associated with comparatively less CO and higher TPR (Tomaka, Blascovich, & Kelsey, 1993). These responses were thought to index threat states. To test for the possible bidirectionality of these responses, these physiological states were engendered with nonpsychological events—specifically, exercise (challenge) or cold pressor (threat)—to determine whether appraisals associated with challenge and threat would follow from the physiological responses (Tomaka, Blascovich, Kibler, & Ernst, 1997). Results showed that although appraisals preceded CV responses as described above, the relationship was not invariant. That is, physiological responses engendered in nonpsychological ways did not influence subsequent appraisals.

Challenge and threat theory has been used in a variety of social and personality domains. In the social domain, these indices have been explored to examine responses within a dyadic social interaction when one member of the dyad is stigmatized in some way. Stigmas were operationalized as physical stigmas (e.g., birthmarks), stigmas resulting from group membership (e.g., race/ethnicity), or socially constructed stigmas (e.g., accents, socioeconomic status). Across more than a dozen studies, participants who interacted with stigmatized partners were more likely to exhibit threat (i.e., lower CO and higher TPR) than were those interacting with nonstigmatized partners. If the results had been found only with physiological responses, they would have still been intriguing—but in many cases the physiological responses also correlated with other automatic or less consciously controlled responses, such as cognitive performance, emotional states, and various nonverbal behaviors (such as freezing, orientation away from the partner, and closed posture) (Mendes et al., 2008; Mendes, Blascovich, Hunter, Lickel, & Jost, 2007; Mendes, Blascovich, Lickel, & Hunter, 2002). Also of interest was the lack of correlations between participants' CV responses and their self-reported appraisals and partner ratings. In contrast with the CV responses, self-reported partner ratings showed a preference for stigmatized over nonstigmatized partners, suggesting that deliberate and consciously controlled measures may be more vulnerable to attempts to correct for racial bias (Blascovich, Mendes, & Seery, 2002; Mendes & Koslov, 2008).

In the personality domain, these measures have been used to assess individuals' reactions to stressful situations. For example, individuals who scored higher on scales assessing belief in a just world (e.g., the view that hard work is rewarded) tended to exhibit greater increases in cardiac and decreases in TPR during stressful tasks than those who scored lower on these scales, who exhibited lower CO and higher TPR—consistent with threat profiles (Tomaka & Blascovich, 1994). Self-perceptions in the form of level and stability of self-esteem have been explored with these methods as well (Seery, Blascovich, Weisbuch, & Vick, 2004). For participants with high and stable self-esteem, positive performance feedback resulted in more challenge responses than for those with high and unstable self-esteem.

Loneliness also appears to result in these patterns of CO and TPR (Cacioppo, Hawkley, & Crawford, 2002; Hawkley, Burleson, & Berntson, 2003). Cacioppo and colleagues (2002) have shown in various settings that individuals reporting higher levels of loneliness are likely to show lower CO and higher TPR than individuals reporting lower levels of loneliness. This effect has been found both in lab-based studies in response to social evaluation, and in field studies using ambulatory impedance and BP devices. In one field study, due to lack of ability to determine whether individuals were actually in motivated performance situations, the authors interpreted these profiles as indicating passive versus active coping styles (Sherwood et al., 1990), with lonely individuals adopting more passive coping styles within the context of their day.

Blood Pressure

Social psychologists have used BP to index several psychological states, including stress, threat, and effort. Much evidence has been accumulated by Wright and colleagues (see Wright & Kirby, 2001, for a review) supporting their theory of effort mobilization. In this extension of Brehm's motivational intensity analysis, it has been empirically demonstrated that participants' effort increases monotonically with difficulty until the task is perceived as too difficult, and then effort is withdrawn. Ability is also a critical factor; when individuals have lower levels of ability, effort is withdrawn at lower levels of difficulty. In this model, Wright's group typically uses SBP as a measure of effort. Although HR and DBP may also follow patterns similar to those for SBP, SBP is thought to be more closely aligned with effort, given its tighter relationship to the sympathetic component of the cardiac cycle (systole).

Experimental Design Considerations

Before incorporating ANS responses into the methodological toolbox, one should consider several important issues that are reviewed here. These considerations include the level of inference one can draw; the complex relationship between the sympathetic and parasympathetic nervous systems; the nature of the experimental context and task; the ways in which health and aging can influence responses; individual and situational stereotypy; the need for knowledge of biological systems; and guidelines for data editing.

Establishing Level of Inference

It is critical to begin with the first major obstacle to any psychophysiologist, which is determining the level of psychological inference that can be attributed to any physiological response. "Inference," in this context, refers to the extent to which an observed physiological response or constellation of responses indicates the presence, absence, or intensity of a psychological state. Here I summarize the main points of psychological inference, and suggest what social and personality psychologists should and should not expect from incorporating ANS responses into their methodological toolboxes.

When one is interpreting physiological responses in terms of what the changes might reflect psychologically, it is useful to evoke the taxonomy of physiological responses outlined by Cacioppo, Tassinary, and Berntson (2000). In this conceptualization, the level of inference is determined by (1) the generality of the context in which the response occurs, and (2) the specificity of the physiological response in relation to the psychological state. The context distinction focuses on whether the context is free and unconstrained (context-independent) or constrained (context-dependent). That is, does one expect that only in a specific context a psychological state would correlate with a physiological response (constrained), or that in any context the psychological–physiological relationship would emerge (unconstrained)?

The specificity dimension refers to the relationship between psychology and physiology. Do many psychological states relate to a physiological response, or do the psychology and physiology have a one-to-one relationship? For example, many psychological states are thought to bring about an increase in SC (e.g., arousal, attention, fear, anxiety); this would be an example of a many-to-one relationship. In contrast, the relationship between negative affect and potentiated startle responses is thought to reflect a one-to-one or invariant relationship. When individuals are experiencing negative emotions, either elicited incidentally or evoked via images, an auditory or visual probe is presented that potentiates the startle response, as evidenced by increased eyeblink magnitude and shortened latency to blink.

When these dimensions of context and specificity are combined, various levels of psychophysiological relationships emerge. When the context is constrained, many-to-one relationships are referred to as "outcomes," whereas one-to-one relationships are referred to as "markers." In an unconstrained context, many-to-one relationships are called "concomitants," and one-to-one relationships are referred to as "invariants." Knowledge of the level of inference is essential to interpreting the psychological meaning of any physiological response.

An additional question related to determining inference is this: What is the "gold standard" for evaluating whether a physiological response is indexing the psychological state of interest? In a somewhat tautological argument, the inferences of physiological responses are often determined by their relationship to a self-reported psychological state. Following the confirmation of the established relationship, some psychophysiologists then will conclude that their physiological responses are revealing responses that are closer to the true and valid experience of the respondents, ignoring the fact that self-reports are often used to establish inference in the first place. Determining psychophysiological inference should be a dynamic process that includes testing and validating relationships between psychology and physiology, and examining the predictive validity of physiological responses to behavior, performance, and health. Most importantly, however, one should not infer that physiological responses *are* the psychological constructs.

Autonomic Space

A second critical factor in examining ANS responses is an understanding of how the sympathetic and parasympathetic branches of the ANS interact and influence each other. In a seminal paper, Berntson, Cacioppo, and Quigley (1991) outline the importance of considering the complexity of the relationships between the two branches. The idea that the sympathetic and parasympathetic branches are reciprocally related (as sympathetic activation increases parasympathetic activity decreases) has been deemed overly simplistic. Instead, it is more accurate to construe these systems as complementary and complexly interactive. For example, increases in sympathetic activation can be associated with decreases in parasympathetic responses; however, this is not exclusively the case. Instead, the systems can be reciprocal, coactivated, or decoupled. An understanding of these relationships can protect against inaccurate conclusions when one system is being observed in the absence of the other. For example, increases in HR may be incorrectly interpreted as reflecting an increase in sympathetic activation, when instead HR increases are due to parasympathetic withdrawal or to a combination of activations in both branches.

Nature of the Experimental Context and Task

The characteristics of the experimental context and task play an important role in the choice of an ANS measure, as well as in how the data are collected, quantified, and (most critically) interpreted. When one is incorporating ANS measures in an experiment, among the first decisions to make is the context in which to collect ANS responses. As described earlier, many of the inferences that can be drawn from the physiological responses are context-bound. For example, although the SCRs that Olsson and colleagues (2005) used in their fear conditioning paradigm are broadly recognized as indexing a fear response, SCRs are by no means universally accepted as indexing fear responses. Indeed, SCRs can result from strong positive emotion, anxiety, deception, attention, and other psychological factors that are certainly distinct from fear. So it is important to know whether a physiological response is believed to be context-bound or context-free. As the context becomes more constrained, one can imagine that the inference level is likely to be increase, though little has been written on this topic.

One of the critical context distinctions in examining ANS responses is the extent to which the participant is engaged in an active versus a passive task (Obrist, 1981). Active tasks are ones in which some response is required from participants, as opposed to passive tasks, in which participants simply experience some event without necessarily having to respond in some instrumental way. This distinction is critical, because in many cases ANS changes are functional; that is, they are responses to the required needs of a task, rather than reflecting the psychological change brought on by the situation. For example, giving a speech requires modulation of respiration to produce vocal tones, and often postural changes are made to improve vocal projection; both of these can influence ANS responses that have nothing to do with stress, emotion, or motivation. In addition, many ANS patterns or profiles are thought to index psychological states stemming from active situations and not passive ones. Challenge and threat, for example, are thought to occur only in active situations and not passive ones. So either watching a scary movie or giving a talk to a room filled with people who disagreed with the speaker might be terrifying, but only in the latter case would the ANS responses yield a pattern associated with threat.

Health of Participants and Individual Response Stereotypy

Recruiting participants for psychophysiology studies poses some challenges. Depending on the response of interest, some health conditions may need to be considered and screened. Of course, when the interest is in HRV or other CV responses, people with heart conditions, pacemakers, or cardiac-altering prescriptions (e.g., beta-blockers) should be excluded. This is probably also true of doctor-diagnosed arrhythmias, though in the 10 years that I have been running participants (resulting in over 3,000 participants), my colleagues and I did not detect any abnormalities on the ECG waveform for the few participants who claimed to have an arrhythmia. Instead, in a small number of cases when participants have claimed *not* to have an arrhythmia, we have noted ECG abnormalities (e.g., bradycardia and premature ventricle contractions). What to do when an arrhythmia is detected is actually a matter of debate (see Stern, Ray, & Quigley, 2003). One perspective is that if a nonmedical professional informs a participant of possible ECG abnormalities and causes undue distress, only to be proven wrong when the person does have a medical screening, this would outweigh the risk of occasionally being correct. The other perspective is that abnormalities can be detected in ECG waveforms, and that an informed opinion about these could be beneficial to participants, so they should be told. Decisions to report should be guided by the policy of the local institutional review board, as well as by the quality of one's knowledge of ECG abnormalities. For several years, I received advice from a cardiovascular surgeon when I was concerned about possible cardiac abnormalities. Forging a relationship with a medical professional may be critical if the institutional review board or funding agency wants any detected abnormalities to be reported to participants. Importantly, though, undergraduate research assistants with limited experience and graduate students just starting their careers should not make these decisions, and each lab should have some plan for how to deal with these possible situations.

For social psychologists, another potential source of difficulties with participants is individual response stereotypy. That is, for some individuals' ANS responses will not be modulated by the experimental situation, no matter what it is. For example, some individuals are thought to be chronic vasoconstrictors and, regardless of the situation, will show constriction rather than dilation in their arteries and arterioles in any change from homeostasis. There is considerable disagreement in the literature regarding the percentage of individuals who respond without psychological modulation, but it is something that could add error and reduce the ability to detect differences based on the experimental manipulation. Certainly older participants are more likely to have sluggish responses and tend to have more individual response stereotypy than younger persons do. Overweight individuals may also show less psychological modulation.

Situational Stereotypy

Parallel with the idea that some individuals respond in stereotyped ways without the influence of the social setting, some situations are thought to bring about stereotyped responses without individual modulation. One of the most obvious situations is the startle reflex, in which sound or visual presentations occur at such high decibels or lumens that the eyeblink reflex occurs for everyone. At lower levels of sound, for example, psychological modulation can occur, so only at intense levels is the startle response universal.

The Need for Knowledge of Biological Systems

The most common question I hear from researchers considering incorporating psychophysiology into their methodological toolboxes is "How much physiology do I need to know?" There is really only answer to this question: "As much as possible." A good understanding of biological systems will inform research questions, choices of context, and (probably most importantly) interpretations of the data. The good news is that obtaining training in biological systems generally and the ANS specifically is easier than some readers may think. Biology departments often have terrific courses in anatomy and physiology. Auditing a medical school class on the CV system can provide invaluable information. Joining such organizations as the SPR and the American Psychosomatic Society, and attending their conferences, can immerse psychologists in a world that does not consider the ANS a mere tool for answering research questions related to social and personality questions; instead, this system *is* their research question. The ways in which the body responds to stress, emotion, temperature changes, age, and other factors differently or similarly are some of the critical issues. Indeed, one might not want to claim brazenly that one is merely interested in ANS measures as mere methods of obtaining answers to psychological research questions. Examining the ANS and the complexities of all its changes is a worthy pursuit in its own right and provides important foundational work for social and personality psychologists whose interest in the system may be merely methodological.

Guidelines for Data Editing

Though one can find many software programs that can edit, score, and ensemble data with a push of the button, I strongly advocate either designing one's own software or scoring the data manually whenever possible. Putting trust in any software program, even those designed by researchers at the top of the field, is a leap of trust that one might not want to make when considering the multiple problems that might arise during data collection. Also, there is nothing quite like editing data to make one appreciate how the system reacts to stimuli, stressors, or events. In addition, after reviewing over a dozen software programs to score impedance waveforms, for example, I have yet to see a program that can consistently detect one of the critical inflection points on the $\Delta z/\Delta t$ waveform—the B point. Under- or overestimating this point can dramatically change SV and CO measures.

We have established several guidelines in my lab to determine the quality of the data while scoring. One guiding rationale is "physiological plausibility." Each measure has a range of responses that are plausible, given the physiological marker. In addition to the plausibility of any single measure, there is the plausibility of a constellation of related measures. Table 7.1 shows plausible ranges of PEP, HR, and LVET (left ventricle ejection time—time from the aortic valve opening to its closing). These relationships demonstrate that when the heart is beating faster, decreases in PEP and LVET can be expected. These ranges are not presented as the only possible ranges that could occur, but rather general guidelines for determining whether the data are typical or not. When scoring or examining data, one should be aware of general ranges in which these measures are related to each other.

Future Directions

One of the greatest advantages of ANS recording is one that has probably been underexamined: testing the dynamic nature of changes in ANS responses as a result of moment-to-moment changes in experience. In many cases, psychophysiologists spend a great amount of time and effort reducing their data to a reasonable number of time epochs and critical responses. However, such statistical techniques as hierarchical linear modeling and time series analyses allow researchers to model tem-

TABLE 7.1. Plausibility of Physiological Ranges: HR, PEP, and LVET

HR (bpm)	PEP (msec)	LVET (msec)
40–60	100–140	300–450
60–80	90–130	250–400
80–120	80–120	250–350
100–120	70–100	200–300
120+	<80	180–300

poral changes in a more fine-grained fashion than ever before (Vallacher, Read, & Nowak, 2002). An additional benefit of these online responses is that they do not require a conscious assessment of what participants are thinking or feeling. Thus responses can be viewed as relatively automatic and less consciously controlled than online subjective reports obtained with rating dials.

Moreover, ANS responses are not limited to lab-based designs. Advances in ambulatory monitoring allow responses to be collected continually throughout a person's daily life and coordinated with experience-sampling techniques. Ambulatory monitoring of ANS responses presents infinite possibilities for social and personality psychologists, particularly those whose work intersects with public health, clinical science, and organizational behavior. The possibilities are endless and limited only by researchers' finances, imagination, and knowledge. I am hopeful that this chapter has offered at least some initial inspiration for expanding the latter two limits.

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nges: HR, PEP, and LVET

LVET (msec)
300–450
250–400
250–350
200–300
180–300

than ever before (Vallacher, of these online responses ssment of what participants be viewed as relatively auto- online subjective reports

ed to lab-based designs. sponses to be collected con- ordinated with experience- of ANS responses presents psychologists, particularly health, clinical science, and endless and limited only owledge. I am hopeful that inspiration for expanding

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