Chapter 6 Measurement of the Human Stress Response



In the final analysis, the empirical foundation of epistemology is measurement.

When an unexplained phenomenon, such as a stress-related disease, is first observed, it is common to search for possible etiological factors. This search often culminates in a phenomenological theory; in this case, perhaps a theory of stress arousal and subsequent pathogenesis. On the basis of the formulated theory, for example, of stress arousal, it is then a useful next step to design an experiment in order to test the theory and any proposed relationships critical to the theory. Inherent in the design of the experiment is the designation of key variables and some means of measuring, recording, or otherwise quantifying those relevant variables. Relevant to the present discussion, this would typically involve a means of measuring the stress response and perhaps its pathological effects.

As we review both the seminal as well as the current literature concerning human stress, it is obvious that in addition to the lack of a universal definition of stress, the field has also been plagued by a plethora of inconsistencies and potential phenomenological errors in the measurement of the human stress response. If we cannot reliably and validly measure the human stress response, what degree of credibility do we place upon investigations into its phenomenology? Indeed, meta-analytic research has suggested that the measurement of independent and dependent variables may be the single most important aspect of research designeven more important than the structure of the research design itself (Cohen, 1984; Fiske, 1983; Smith, Glass, & Miller, 1980). With regard to stress research, it may be argued that the confounded or inappropriate measurement process has the greatest ability to limit the generation of useful data regarding this important public health phenomenon. This view was appreciated by early writers (see Cattell & Scheier, 1961; Everly & Sobelman, 1987; Stamm, 1996). Thus, the purpose of this chapter is to discuss the measurement of the human stress response. In doing so, we shall review the seminal scales, the transitional, and the extant scales. We provide the historical perspective to the reader so as to provide glimpse of the evolution of the measurement process itself. Such tact also provides insight into what researchers viewed as salient as well as accessible.

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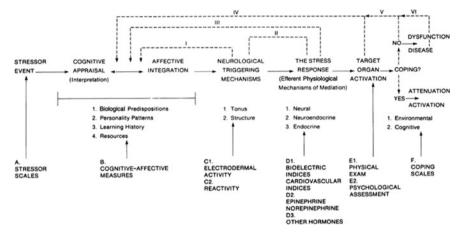


Fig. 6.1 Measurement of the human stress response

In Chap. 2, a system's model of the nature of the human stress response was constructed (Fig. 2.6). As a means of integrating the following measurement-based discussions, that basic model is reproduced here, with key measurement technologies having been superimposed (see Fig. 6.1). Let us take this opportunity to examine more closely the measurement of the human stress response.

Stressor Scales

Historically, one of the most widely used measurement tool for the assessment of human stress, in reality, does not measure stress at all—it measures stressors. The Social Readjustment Rating Scale (SRRS), the "grandfather" of attempts at measuring stress, was developed by Holmes and Rahe (1967), based upon the theory that "life change" is causally associated with subsequent illness. This notion was by no means a new idea. Adolph Meyer pioneered empirical investigations into the relationship between psychosocial events and illness with the advent of his "life chart" as a means of creating a medical history.

The SRRS contains 43 items consisting of commonly experienced "life events." Each life event is weighted with a life change unit score (LCU). Respondents are simply asked to check each of the items they have experienced within the last 12 months. The arithmetic summation of LCUs represents the total LCU score, which can then be converted to a relative health risk statement, that is, the risk of becoming ill within a stipulated time period. The association between high LCU scores and risk of subsequent illness is assumed to be a function of the fact that organisms must adapt to novel stimuli and otherwise new life events.

physiology of adaptation has long been known to be the same physiology as the stress response. Thus, stress may be seen as the linchpin between life events and illness as conceived of and measured by the SRRS.

The SRRS is not without its critics, however. Two major issues have been raised:

- 1. Life events scales should be modified so as to assess the perceived desirability of the life event. It has been suggested that negative life events are potentially more pathogenic than positive life events (Sarason, Johnson, & Siegel, 1978).
- 2. It has also been suggested that "minor hassles" are more important predictors of illness than major life events (Kanner, Coyne, Schaefer, & Lazarus, 1981).

Other noteworthy efforts in the assessment of stressor stimuli should be mentioned. In an attempt to improve the SRRS with regard to the issue of event desirability, Sarason and his colleagues (1978) created the Life Experiences Survey (LES), which not only lists a series of life events but also inquires into the desirability of each of the events. In a far more ingenious approach to the life events issue, Lazarus and his colleagues investigated the daily hassles versus major life events issue as it pertains to the prediction of subsequent illness (Kanner et al., 1981). The Hassles Scale lists a series of minor daily hassles, that is, sources of frustration that commonly recur to many individuals. The scale also includes an "uplifts" assessment that theoretically serves to mitigate the adverse impact of negative life events.

The LES and the Hassles Scale are creative and alternative approaches to the assessment of stressors. Another entry into the genre of stressor scales is the Stressful Life Experiences Screening (SLES; Stamm, 1996). This instrument consists of 20 items that inquire as to (1) the presence of a stressful life experience, and (2) the degree of "stressfulness" of that experience. The long form (SLES-L) takes 5–10 min to complete.

The Life Stressor Checklist—Revised (Wolfe & Kimerling, 1998) consists of 30 "events" that satisfy The *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-4*; American Psychiatric Association [APA], 1994) definition of traumatic and presumably approximate *DSM-5* (APA, 2013) stressors, although the *DSM-5* A criterion has been broadened. The self-report scale takes 15–30 min to complete and is designed for use with adults. The scale is not only an indicator of traumatic events, but it also serves as an assessment of the events' current impact upon the individual.

The Stress and Adversity Inventory (STRAIN) was created by the University of Los Angeles's Laboratory for Stress Assessment and Research (Slavich & Epel, 2010). This is a computerized self-report inventory that consists of 96 questions that cover moderate to severe stressors that are typically experienced by the adult population. The strain is designed for use with adults and takes approximately 30–45 min to complete.

As for the genre of stressor scales, Monroe (1983) notes, "Although findings of event—illness associations appear to be consistent in that increased life events predict dysfunction in both retrospective and prospective studies, the magnitude of

the association reported typically has been low" (p. 190). The recognized consistency in the life events research combined with its low-effect size leads one to believe that life events scales such as the SRRS do indeed tap some domain that has meaning in stress phenomenology; however, there appear to be other mediating variables that need to be better understood. From the view of the present model, life events scales tap the stressor domain and therefore cannot be said to assess either the stress response itself or the causal mechanisms that undergird stress arousal. Nevertheless, scales such as the SRRS can be of value, especially in stress research when the researcher wishes to obtain valid and reliable assessments of the "background noise," that is, intervening or other otherwise confounding variables in psychosocial stressor research (see Everly & Sobelman, 1987).

Cognitive–Affective Correlate Scales

Whereas in the preceding section we discussed the assessment of stressor stimuli, the reader will recall from Chap. 2 the agreement among most stress researchers that in order for psychosocial life events to engender a stress response and subsequent illness, they must first be processed via cognitive–affective mechanisms. It seems theoretically viable, therefore, that one might assess the cognitive–affective domain of respondents as an indirect assessment of the human stress response (Everly & Sobelman, 1987). Derogatis (1977) has argued that such a "self-report mode of psychological measurement contains much to recommend it" (p. 2). Furthermore, Everly has argued that assessment of this domain may be the most practical, efficient, and cost-effective way of measuring the human stress response (Everly & Sobelman, 1987; Everly, Davy, Smith, Lating, & Nucifora, 2011; Nucifora, Hall, & Everly, 2011).

The World Assumptions Scale (WAS; Janoff-Bulman, 1996) assesses three core assumptions, or beliefs, about life: the benevolence of the world, the inherent meaningfulness of the world, and self-worth. This self-report scale requires 5–10 min to complete and consists of 32 items scored according to a 6-point Likert scale. Although the issue of temporal instability has been raised with this scale (Kaler et al., 2008) it still may provide useful information regarding core beliefs that may serve as vulnerabilities for traumatic exposures.

The Stress Arousal Scale (SAS4) is a scale that has been utilized and refined for over 40 years to its current four item form (Everly, Sherman, & Smith, 1989; Smith, Everly, & Haight, 2012). It is based upon the perseverative cognition hypothesis that states obsessive reiterative ideation is pathogenic. The SAS4, in a series of studies over four decades, has demonstrated that obsessive worry is indeed pathogenic. Through advanced structural equation modeling, the SAS4 has been shown to be a powerful predictor of emotional exhaustion, burnout, avoidance, and job dissatisfaction. It has also been shown to predict physical illness. The SAS4 is ideally suited to be part of a larger battery or to be used as a brief screen.

Neurological Triggering Mechanisms

The assessment of the sensitivity of neurological triggering mechanisms is by no means an easy task. Aberrant-evoked potentials emerging from the subcortical limbic system would be one indication of an existing hypersensitivity phenomenon within the limbic system. The accurate assessment of subcortical activity via electroencephalography (EEG) is very difficult and may be considered a gross assessment at best, however. False-negative findings are a common problem with such assessment and EEGs in general. Electrodermal responsiveness as assessed via galvanic skin response (GSR) would be another way of assessing the reactivity of neurological triggering mechanisms (Peek, 2003).

Finally, the general assessment of psychophysiological reactivity is believed to be a viable process for assessing the efferent-discharge propensity of the limbic system. Everly and Sobelman (1987) provided an early summary of measurement approaches to this domain. Potter and Bolls (2012) have a useful and practical review, while Cacioppo, Tassinary, and Berntson (2017) provide the most up-to-date and scholarly analysis of this domain. The phenomenology of this process is based upon the theories of Lacey, Malmo, and Sternbach discussed in Chap. 4 and further refined in Potts and Bolls (2012) and Cacioppo, Tassinary, and Berntson (2017).

Measuring the Physiology of the Stress Response

It will be recalled from Chap. 2 that the stress response can be divided into three broad categories: (1) the neural axes, (2) the neuroendocrine axis, and (3) the endocrine axes. Let us briefly review several of the more common assessment technologies used to tap these phenomenological domains. Further insight will be gained by a careful review of Cacioppo et al. (2017). In their state-of-the-art analysis, they review not only the measures below but extend into neuroimaging, behavioral genetics and epigenetics, and psychoneuroimmunology, much of which is beyond the scope of our presentation but serves as useful adjunctive material.

Assessment of the Neural Axes

Assessment of the neural axes of the human stress response is for the most part an attempt to capture a transitory state measurement phenomenon, as opposed to a more consistent trait. Technologies used for such assessment include (1) electrodermal techniques, (2) electromyographic techniques, and (3) cardiovascular measures.

Electrodermal Measures

The physiological basis of the electrodermal assessment of the stress response is the eccrine sweat gland. Located primarily in the soles of the feet and the palms of the hands, these sweat glands respond to psychological stimuli rather than heat and emerge on the terminal efferent ends of sympathetic neurons. Although the neurotransmitter at the sweat gland itself is Ach, as opposed to NE, the assessment of this activity provides useful insight into the activity of the sympathetic nervous system. Electrodermal activity may be assessed via active GSR techniques or through passive techniques such as skin potentials (SP), according to Edelberg (1972). Andreassi (1980a, 1980b) has stated that electrodermal techniques are useful indices of somatic arousal.

Electromyographic Measurement

The physiological basis of electromyographic measurement of the stress response is the neurological innervation of the striated skeletal muscles. Electromyography, although an indirect measure of muscle "tension," is a direct measure of the action potentials originating from the neurons that innervate the muscles.

Skeletal muscles receive their neural innervation primarily as a result of alpha-motoneuron presence, on the efferent limb, and secondarily as a result of gamma-motoneuron activity as well. From the afferent perspective, proprioceptive neurons arising from the muscle spindles contribute to the overall electrical activity that originates from the skeletal musculature. In a relaxed state, skeletal muscle tone serves as a very useful general index of arousal (Gellhorn, 1964; Gellhorn & Loofburrow, 1963; Jacobson, 1929, 1970; Malmo, 1975; Weil, 1974), yet; in a contracted state, this utility appears to disappear. Thus, when using skeletal muscles as general indices of arousal and stress responsiveness, it becomes of critical importance to teach patients to first relax those muscles (Everly, Welzant, Machado, & Miller, 1989).

There has been debate on the utility of a particular set of muscles as an index of arousal. That set of muscles is the group known as the *frontalis*. Jacobson (1970) and Shagass and Malmo (1954) first recognized that the frontalis and related facial muscles were prime targets of the stress-arousal process. Budzynski and Stoyva (1969) and Stoyva (1979) explored and refined the clinical utility of these muscles in the treatment of stress-related disorders. Similar work was undertaken by Schwartz et al. (1978), who found the corrugator muscles of similar utility in relation to depression.

It may be argued that the frontalis muscles of the forehead provide a useful site for the assessment of stress arousal. These muscles have been termed "quasi-voluntary" muscles because their autonomic-like properties manifest during emotional states. In support of such a view are the studies indicating that when simple facial expressions are mimicked, an alteration in heart rate and skin temperature can be observed, even when the subjects were simply asked to mimic the expression without any consideration for the cognitive or affective state that might be associated with it. Similarly, Rubin (1977) suggests that the frontalis muscles, in particular, may possess properties of dual innervation: skeletal alpha-motoneuron and ANS innervation.

Although, clearly, the frontalis musculature is predominately striated in nature (thus receiving efferent innervation from the alpha-motoneuron assemblies). Rubin (1977) has argued that the frontalis also possesses thin nonstriated layers of musculature. These nonstriated muscles apparently receive their innervation (directly or indirectly) from the SNS (Miehlke, 1973). Thus, assessment of the frontalis muscles through electromyographic procedures may well provide insight into alpha-motoneuron activity, sympathetic neural activity, as well as neuroendocrine activity (Everly & Sobelman, 1987). Although there is not total agreement on the utility of the frontalis musculature (Alexander, 1975), Stoyva (1979) provides useful guidelines for the use of that measurement variable. Also see Potter and Bolls (2012) and Cacioppo et al. (2017) for state-of-the art reviews.

Clinical biofeedback experience shows the frontalis muscles are useful in the treatment of a wide range of stress-related disorders, including essential hypertension and disorders of the GI system. Most clinicians, over the years, have reported use of the frontalis muscle in electromyographic assessment; however, the trapezius, brachioradialis, and sternocleidomastoid muscle groups have also been utilized.

In summary, most evidence suggests that the electromyographic assessment yields insight into the activity of other major muscle groups (Freedman & Papsdorf, 1976; Glaus & Kotses, 1977, 1978) as well as the generalized activity of the SNS (Arnarson & Sheffield, 1980; Budzynski, 1979; Donaldson, Donaldson, & Snelling, 2003; Field, 2009; Jacobson, 1970; Malmo, 1966; Rubin, 1977; Schwartz & Andrasik, 2003).

Cardiovascular Measurement

Cardiovascular measurement of the stress response entails the assessment of effects of the stress response upon the heart and vascular systems. Common cardiovascular measures include heart rate, peripheral blood flow, and blood pressure.

Heart rate activity as a function of the stress response is a result of direct neural innervation as well as neuroendocrine activity of epinephrine and norepinephrine. During psychosocially induced stress, epinephrine is preferentially released from the adrenal medullae. The ventricles of the heart are maximally responsive to circulating epinephrine and will respond with increased speed and force of ventricular contraction. Of course, direct sympathetic neural activation increases heart rate as well. The measurement of heart rate is most commonly achieved through the use of audiometric or oscillometric techniques during the normal assessment of blood pressure. Occasionally, heart rate will be measured from ECG techniques via the use of passive electrodes or even through plethysmography.

Plethysmography focuses upon the volume of blood in a selected anatomical site. The most common areas for such assessment of the stress response are the fingers, toes, calves, and forearms. During the stress response, most patients will suffer a reduction of blood flow from these areas. This vasoconstrictive effect is a result of direct sympathetic activity to the arteries and arterioles, as well as of circulating norepinephrine (Hall, 2011). A decline of blood flow to these areas will also result in a reduction of skin temperature. Therefore, skin temperature is also sometimes utilized, although it is not as reliable as plethysmography. So we see that the assessment of peripheral blood flow can be accomplished via the use of plethysmography as well as skin temperature.

Finally, blood pressure is sometimes used as an *acute* index of the stress response. The assessment of blood pressure is generally achieved through the quantification of systolic and diastolic blood pressure and may be considered highly state-dependent.

Systolic blood pressure is the hemodynamic pressure exerted within the arterial system during systole (the ventricular contraction phase). Diastolic blood pressure is the hemodynamic pressure exerted within the arterial system during diastole (relaxation and filling of the ventricular chambers).

Blood pressure is a function of several variables revealed in the following equation:

$$BP = CO \times TPR$$

where

BPblood pressureCOcardiac output = stroke volume \times heart rate

TPR total hemodynamic peripheral resistance

Blood pressure can be measured noninvasively through auscultation, audiometry, or oscillometry. In noninvasive paradigms, a sampled artery (usually the brachial) is compressed through the use of an inflatable rubber tube or bladder. The bladder is inflated until it totally blocks the passage of blood through the artery. Air pressure, measured in millimeters of mercury (mm Hg), is slowly released from the bladder until a sound is heard or a distension sensed. This sound and distension (called a Korotkoff sound) is indicative of blood being allowed to pass through the once blocked artery. Korotkoff sounds continue until the artery is fully opened and returned back to its natural status. The first Korotkoff sound is indicative of the systolic blood pressure. The passing of the last Korotkoff sound is indicative of the diastolic blood pressure. The technique of audiometry measures blood pressure by the use of a microphone to sense the Korotkoff sounds. Oscillometry detects the Korotkoff phenomenon via a pressure-sensitive device placed on the outside of the artery. Finally, auscultation is the sensing of the Korotkoff sound via stethoscope. Audiometric and oscillometric techniques are far more reliable than is manual auscultation.

In recent years, heart rate variability (HRV) has emerged as an inexpensive, useful, and pragmatic means of measuring stress in the cardiovascular system (Thayer & Sternberg, 2006). HRV represents the variation in the timed interval between heartbeats (variation in the beat-to-beat heart rate interval). Declines in variability are usually indicative of increased stress because of the presence of catecholamine cascades. These cascades tend to overwhelm normal variabilities (Sharma & Gedeon, 2012) in response to physical or psychogenic challenges. HRV is associated with declines in executive function and mortality (Kleiger, Miller, Bigger, & Moss, 1987; Nickel & Nachreiner, 2003). HRV is most commonly measured using a photoplethysmograph (PPG). It is practical and inexpensive. More accurate measurements may be derived from an electrocardiogram. This measurement is considered superior because it makes it easier to identify heartbeats not originating in the sinoatrial node thus excluding ectopic pacemakers. Practicality is sacrificed, however. There is even now a HRV app available commercially.

In summary, the measurement of cardiovascular phenomena can be seen to tap both neural and neuroendocrine domains; thus, there is an overlap in phenomenology. Also, when using the cardiovascular domain to measure stress arousal, the clinician is interested only in the *acute* fluctuations, as opposed to chronic levels. This is due to the fact that stress exerts its most measurable effect upon the acute status of the cardiovascular system. A multitude of other factors enter into, and otherwise confound, the measurement process when examining cardiovascular indices such as chronic blood pressure and peripheral blood flow, for example, photoplethysmography is easy to use, inexpensive, but vulnerable to factors other than stress such as posture and room temperature (Sharnma & Gedeon, 2012).

Assessment of the Neuroendocrine Axis

Assessment of the neuroendocrine axis of the stress response entails measurement of the adrenal medullary catecholamines: epinephrine (adrenaline) and norepinephrine (noradrenaline).

Aggregated medullary catecholamines may be sampled from blood or urine and assayed via fluorometric methods. Reference values range for random sampling up to 18 μ g/100 ml urine, for a 24-h urine sample up to 135 μ g, and for timed samples, 1.4–7.3 μ g/h during daylight hours (Bio-Science, 1982). For aggregated catecholamines sampled from plasma, values range from 140 to 165 pg/ml via radioenzymatic procedures (Bio-Science).

Various fluorometric (Anderson, Hovmoller, Karlsson, & Svensson, 1974; Euler & Lishajko, 1961; Jacobs et al., 1994), chromatographic (Jacobs et al., 1994; Lake, Ziegler, & Kopin, 1976; Mason, 1972), and radioimmunoassay (Jacobs et al., 1994; Mason, 1972) methods are available for the assessment of catecholamines. The most useful of all methods may be the high-pressure liquid chromatography (HPLC) with electrochemical detection as described in Hegstrand and Eichelman (1981) and McClelland, Ross, and Patel (1985). HPLC allows multiple

catecholamines to be derived from sampled plasma, urine, and saliva with superior ease and sensitivity (Peaston & Weinkove, 2004; Tamano, Ishida, Asaki, Hasegawa, & Shinohara, 2016).

Epinephrine can be sampled from urine, plasma, or saliva. When sampled from urine a typical distribution is as follows: (see Jacobs et al., 1994; Katzung, 1992):

Unchanged epinephrine	6%
Metanephrine	40%
Vanillylmandelic acid	41%
4-Hydroxy-3-methoxy-phenylglycol	7%
3,4-Dihydroxymandelic acid	2%
Other	4%
	100%

Norepinephrine can also be sampled from urine, plasma, and saliva. Table 6.1 provides a range of epinephrine and norepinephrine values when sampled from urine.

Despite the availability of methods such as HPLC, some researchers prefer the assessment of catecholamines by indirect routes, for example, through the assessment of urinary metabolites. Metanephrines and vanillylmandelic acid (VMA) are two popular choices.

In the case of the metanephrines, one of the major deactivating substances acting upon epinephrine and norepinephrine is the enzyme catecholamine-*O*-methyl-transferase (COMT). Metabolites of this deactivation process are metanephrine and normetanephine. Aggregated metanephrines range from 0.3 to 0.9 mg/day in urine. VMA levels range from 0.7 to 6.8 mg/day. VMA is the urinary metabolite of COMT and monoamine oxidase.

Assessment of the Endocrine Axes

According to Selye (1976), the most direct way of measuring the stress response is via ACTH, the corticosteroids, and the catecholamines. The catecholamines have already been discussed. The most commonly used index of ACTH and corticosteroid activity is the measurement of the hormone cortisol. Cortisol is secreted by the adrenal cortices, activated by ACTH, at a rate of about 25–30 mg/day and accounts for about 90% of glucocorticoid activity.

	Epinephrine (µg/day)	Norepinephrine (µg/day)
Basal levels	4–5	28–30
Aroused	10–15	50-70
Significant stress	>15	>70

Table 6.1 Value ranges for urinary epinephrine and norepinephrine

Cortisol may be sampled from either plasma or urine. Radioimmunoassay plasma levels for a normal adult may range from 5 to 20 μ g/100 ml plasma (8 A.M. sample). The normal diurnal decline may result in a level of plasma cortisol at 4 P. M. about one half of the 8 A.M. level. Normal urinary-free cortisol may range from 20 to 90 μ g/24 h (see Bio-Science, 1982). It has been suggested that urinary-free cortisol is the most sensitive and reliable indicator of adrenal cortical hyperfunction, followed by plasma cortisol and finally 17-hydroxycorticosteroid (17-OHCS), a cortisol metabolite (Damon, 1981). Normal values for 17-OHCS measured from urine typically range from 2.5 to 10 mg/24 h in the female to 4.5 to 12 mg/24 h in the male adult (Porter-Silber method). Slight increases in 17-OHCS are evidenced in the first trimester of pregnancy and in severe hypertension. Moderate increases can be observed in the third trimester of pregnancy and as a result of infectious disease, burns, surgery, and stress (Bio-Science). In conditions of extreme stress, urinary 17-OHCS may exceed 15 mg/24 h. Plasma assessments of 17-OHCS range from 10 to 14 μ g% at 8 A.M. basal levels to 18 to 24 μ g% under moderate stress, to an excess of 24 µg% in extremely stressful situations (see Dettenborn, Tietze, Kirschbaum, & Stalder, 2012; Mason, 1972). Clearly, the result of any hormone assessment will vary depending on medium (hair, blood, urine, saliva) and will also vary between laboratories as assessment techniques will vary as well.

This section has discussed the assessment of the physiological constituents of the stress response. It should be noted that the assessment of this domain represents a challenging and potentially frustrating exercise. One major factor that confounds the assessment of most physiological variables is the fact that most physiological phenomena used to assess stress arousal are state-dependent variables that wax and wane throughout the course of a day as well as with acute situational demands. Normal diurnal fluctuations as well as acute situational variability can serve to yield false-positive or false-negative findings in the absence of meaningful baseline data. There has even been some question as to the predictive validity of acute physiological indices. Another issue that confounds the overall utility of many physiological equipment, or both. The difficulties associated with physiological assessment of the human stress response have been summarized by Everly and Sobelman (1987). Other issues, such as response specificity and organ reactivity, are also reviewed.

Assessment of Target-Organ Effects

Once the stress response has been activated to pathogenic proportions, there emerges another possible assessment strategy for measuring human stress—the assessment of the target-organ effects of the stress response. The assessment of target-organ effects can consist of measuring physical as well as psychological variables.

Physical Diagnosis

The assessment of the physical effects of stress would involve the use of standard diagnostic techniques common to the practice of physical medicine. The goal of such assessments is to measure the integrity of the target organ's structural and functional status. An in-depth discussion of such procedures is far beyond the scope of this volume, however.

It should be mentioned that such assessments are never clearly assessments of stress. One never really knows to what degree pathogenic stress arousal has contributed to the manifestation of target-organ pathology. For this reason, the diagnosis of stress-related target-organ disease is typically a diagnosis by exclusion; that is, one systematically excludes nonstress-related etiological factors while at the same time looking for the evidence of pathogenic stress arousal through the assessment of other measurement domains as well. The stress-related diagnosis then emerges from a convergence of these data sets. There are also self-report scales that have shown to be valid and reliable indices of experienced physical illness. The Seriousness of Illness Rating Scale (SIRS; Wyler, Masuda, & Holmes, 1968) is one useful self-report tool for measuring illness and weighting its impact. The SIRS was updated and revised by Rosenberg, Hayes, and Peterson (1987) and while old by today's standards remains of clinical utility. The Stress Audit Questionnaire (Miller & Smith, 1982) is another. It is important to keep in mind that there is still no certainty as to the extent of the role of stress arousal in the formation of the emergent illnesses/reactions.

Finally, the Family Disruption from Illness Scale (Ide, 1996) extends the assessment of physical symptoms somewhat by assessing the degree of disruption that 53 health-related symptoms impose upon daily functioning. Most items represent physical illnesses. This scale, while more recent than the SIRS, is not as comprehensive, nor have its psychometric properties been adequately assessed.

Psychological Diagnosis

The psychological diagnosis of the stress response refers to the measurement of the "psychological" effects of the stress response. There currently exist numerous and diverse methods for the measurement of psychological states and traits. To cover this topic fully would require a volume of its own. Therefore, what we shall do in this section is merely highlight the paper-and-pencil questionnaires that a clinician might find most useful in measuring the psychological effects of the stress response.

Minnesota Multiphasic Personality Inventory—2

The Minnesota Multiphasic Personality Inventory—2 (MMPI-2) (Butcher, Dahlstrom, Graham, Tellegren, & Kraemmer, 1989) is a revision of perhaps one of

the most valid and reliable inventories for the assessment of long-term stress on the personality structure of the patient. The numerous clinical and content scales of the MMPI-2 yield a wealth of valuable information. These scales sample a wide range of "abnormal" or maladjusted personality traits (a personality trait is a rather chronic and consistent pattern of thinking and behavior).

The MMPI-2 consists of ten basic clinical scales developed on the basis of actuarial data:

- 1. Hs: Hypochondriasis
- 2. D: Depression
- 3. Hy: Conversion Hysteria
- 4. Pd: Psychopathic Deviate
- 5. Mf: Masculinity-Femininity
- 6. Pa: Paranoia
- 7. Pt: Psychasthenia (trait anxiety)
- 8. Sc: Schizophrenia
- 9. Ma: Hypomania (manifest energy)
- 10. Si: Social Introversion (preference for being alone)

In addition to the highly researched clinical scales, the MMPI-2 has validity scales that give the clinician a general idea of how valid any given set of test scores is for the patient. This unique feature of the MMPI-2 increases its desirability to many clinicians.

The MMPI-2 offers a virtual wealth of information to the trained clinician; its only major drawback appears to be its length of over 560 items.

The Sixteen Personality Factor Questionnaire (16-PF)

The 16-PF (Cattell, 1972), much the same as the MMPI, assesses a wide range of personality traits. It measures 16 "functionally independent and psychologically meaningful dimensions isolated and replicated in more than 30 years of factor-analytic research on normal and clinical groups" (p. 5).

The 16-PF consists of 187 items distributed across the following scales:

- Reserved–Outgoing
- Less Intelligent-More Intelligent
- Affected by Feelings-Emotionally Stable
- Humble-Assertive
- Sober–Happy-Go-Lucky
- Conservative-Experimenting
- Group-Dependent-Self-Sufficient
- Expedient-Conscientious
- Shy-Venturesome
- Tough-minded-Tender-minded

- Trusting-Suspicious
- Practical–Imaginative
- Forthright-Astute
- Self-Assured-Apprehensive
- Undisciplined Self-Conflict-Controlled
- Relaxed-Tense.

Millon Clinical Multiaxial Inventory—II

The Millon Clinical Multiaxial Inventory (MCMI) (Millon, 1983) was a 175-item self-report, true–false questionnaire. The MCMI-II, although it was not as widely utilized as the MMPI in the diagnosis of major psychiatric disorders, is clearly the instrument of choice when the clinician was primarily interested in personologic variables and their relationship to excessive stress. Furthermore, the MCMI-II offered valuable insight into treatment planning and was keyed to the then newly emerged *DSM-III* (APA, 1980). Another major advantage of the MCMI-II over the MMPI and 16-PF was that it consisted of only 175 items. The MCMI-II included 22 clinical scales broken down into three broad categories; ten basic personality scales reflective of the personality theory of Theodore Millon (1981); three pathological personality syndromes; and nine major clinical psychiatric syndromes (Millon, 1983). From a psychometric perspective, the MCMI-II offered the best of both worlds: an inventory founded in a practical, clinically useful theory as well as rigorous empirical development. The clinical scales of the MCMI-II are listed below:

Schizoid; Avoidant; Antisocial; Narcissism; Passive–aggressive; Compulsive; Dependent; Histrionic; Schizotypal; Borderline; Sadistic; Paranoid; Anxiety; Somatoform; Hypomania; Dysthymia; Alcohol abuse; Drug abuse; Psychotic thinking; Psychotic depression; Psychotic delusions.

Millon Clinical Multiaxial Inventory—III

Theodore Millon was famous for his inclination to continue to revise and innovate. Thus he updated the MCMI-II by creating the MCMI-III (Millon, Millon, Davis, & Grossman, 2009). The MCMI-III maintained 175 items but 95 were changed or reworded from the MCMI-II.

The authors created *14 Personality Disorder Scales* that were coordinated with the *DSM-IV* (APA, 1994) Axis II disorders:

1—Schizoid 2A—Avoidant 2B—Depressive 3—Dependent
4—Histrionic
5—Narcissistic
6A—Antisocial
6B—Sadistic (Aggressive)
7—Compulsive
8A—Negativistic
(Passive-Aggressive)
8B—Masochistic (Self-Defeating)
S—Schizotypal
C—Borderline
P—Paranoid

In addition there were ten Clinical Syndrome Scales:

A—Anxiety
H—Somatoform
N—Bipolar: Manic
D—Dysthymia
B—Alcohol Dependence
T—Drug Dependence
R—Posttraumatic Stress Disorder
SS—Thought Disorder
CC—Major Depression
PP—Delusional Disorder

There were also five scales that serve to detect response patterns that might call into question the test results: Modifying Indices

- X—Disclosure
- Y—Desirability
- Z-Debasement

Random Response Indicators

- V—Invalidity
- W-Inconsistency

Lastly, there were 42 subscales that served to give the clinician insight into the psychological processes that undergird clinically significant elevations. These were the Grossman Facet Scales.

Millon Clinical Multiaxial Inventory—IV

Although at the time of this publication the MCMI-III was still available, continuing the theme of revision, the authors published the MCM-IV in 2015. It was coordinated with the *DSM-5* (APA, 2013). This current version contains 195 items. The test has four categories of scales:

- 15 Personality Pattern Scales
- 10 Clinical Syndrome Scales
- 5 Validity Scales: 3 Modifying Indices; 2 Random Response Indicators
- 45 Grossman Personality Facet Scales

1-Schizoid

2A—Avoidant

2B—Melancholic

- 3—Dependent
- 4—Histrionic
- 4B—Turbulent
- 5—Narcissistic
- 6A—Antisocial
- 6B—Sadistic (Aggressive)
- 7—Compulsive
- 8A—Negativistic
- (Passive-Aggressive)
- 8B—Masochistic (Self-Defeating)
- S—Schizotypal
- C-Borderline
- P-Paranoid

In addition there were ten Clinical Syndrome Scales:

A—Anxiety

- H-Somatoform
- N-Bipolar: Manic
- D-Persistent Depression
- B—Alcohol Dependence
- T-Drug Dependence
- R-Posttraumatic Stress Disorder
- SS-Thought Disorder
- CC-Major Depression
- PP-Delusional Disorder

The unique strength of the Millon inventories was its validation. In MCMI-II, Millon relied heavily upon discriminate validation expressed in terms of receiver operating characteristics (ROC). He pioneered this approach for usage in large multiscale inventories. This is the gold standard in psychometric assessment in that it is the expression of the probability that a given patient's test score is truly indicative of that person's membership in a given diagnostic category. Operating characteristic expressions of sensitivity, specificity, false-positive error, and false-negative error were of great value clinically. This feature alone made the Millon inventories the preferred choice in forensic setting. As the inventories were revised, greater reliance was placed upon construct validation rather than ROC validation, although much of the original ROC validation is sustained in the MCMI-IV's core personality and clinical syndrome scales as they were sustained across revisions.

Impact of Events Scale—Revised

The Impact of Events Scale—Revised (IES-R) (Weiss & Marmar, 1993) is a revision of the original IES. The IES-R consists of 22 self-report items purported to assess posttraumatic stress. Three response dimensions are tapped: intrusive ideation, avoidance and numbing, as well as hyperarousal. The IES-R takes about 10 min to complete and is a widely used research tool.

Penn Inventory for Posttraumatic Stress Disorder (PENN)

Similar to the IES-R, the PENN (Hammarberg, 1992) is a measure of posttraumatic symptoms. It is, however, is a more global measure, consisting of 26 self-report items.

PTSD Checklist for DSM-5

The PTSD Checklist for *DSM-5* (PCL-5) (Weathers et al., 2013) is a revision of the PCL for *DSM-5*. The PCL-5 consists of 20 self-report items that assess the 20 *DSM-5* (APA, 2013) symptoms of PTSD. Respondents rate each symptom on a scale of 0–4. The checklist takes 5–10 min to complete and can be used to monitor symptom changes, screen individuals for PTSD, and make a provisional PTSD diagnosis.

Life Events Checklist for DSM-5

The Life Events Checklist for *DSM-5* (LEC-5) (Weathers et al., 2013) is a self-report measure that screens for the occurrence of potentially traumatic events within the respondent's lifetime. The LEC-5 screens for exposure to 16 potential PTSD inducing events with an additional item that accounts for particularly stressful events not covered by the prior 16 items. Respondents indicate levels of exposure to each event on a 6-point nominal scale. This measure may be used in combination with other scales in order to confirm exposure to a PTSD Criterion A traumatic event.

Stanford Acute Stress Reaction Questionnaire

The Stanford Acute Stress Reaction Questionnaire (SASRQ) (Cardena & Spiegel, 1993; Shalev, Peri, Canetti, & Schreiber, 1996) consists of 30 self-report items that assess acute stress disorder. The scale takes 5–10 min to complete and appears to be useful in predicting PTSD.

Taylor Manifest Anxiety Scale

The Taylor Manifest Anxiety Scale (TAS) (Taylor, 1953), unlike the inventories previously described, measures only one trait—anxiety. Its 50 items are derived from the MMPI. The TAS measures how generally anxious the patient is and has little ability to reflect situational fluctuations in anxiety.

State–Trait Anxiety Inventory

The State–Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, & Luchene, 1970) is a highly unique inventory in that it is two scales in one. The first 20 items measure state anxiety (a psychological state is an acute, usually situationally dependent condition of psychological functioning). The second 20 items measure trait anxiety. This is the same basic phenomenon as that measured by the TAS. The STAI can be administered in full form (40 items) or be used to measure only state or trait anxiety. It is one of the most widely used anxiety scales in the world despite its age (Julian, 2011). Its strength resides in the dual assessment capability: state and trait anxiety constructs. For those interested in assessment of state anxiety, this scale has the most robust data base.

Affect Adjective Checklist

Another unusual measuring device is the Affect Adjective Checklist (AACL) (Zuckerman, 1960). Like the STAI, the AACL can be used to measure a psychological state or trait by using the same items (21 adjectives) and merely changing the instructions. The client may use the checklist of adjectives to describe how he or she feels in general or under a specific set of conditions—"now" for instance. Zuckerman and Lubin (1965) later expanded the AACL by adding specific items to assess hostility and depression. The more recent (1985) scale is called the Multiple Affect Adjective Checklist (MAACL).

Subjective Stress Scale

The Subjective Stress Scale (SSS) (Berkun, 1962) is designed to measure situational (state) effects of stress on the individual. The scale consists of 14 descriptors that the patient can use to identify his or her subjective reactions during a stressful situation. Each of these descriptors comes with an empirically derived numerical weight, which the clinician then uses to generate a subjective stress score.

Profile of Mood States

The Profile of Mood States (POMS) (McNair, Lorr, & Droppleman, 1971) is a factor-analytically derived self-report inventory that measures six identifiable mood or affective states (p. 5):

Tension-Anxiety Depression-Dejection Anger-Hostility Vigor-Activity Fatigue-Inertia Confusion-Bewilderment

The POMS consists of 65 adjectives, each followed by a 5-point rating scale that the patient uses to indicate the subjective presence of that condition. The instructions ask the patient to use the 65 adjectives to indicate "How you have been feeling during the past week including today." Other time states have been used, for example: "right now," "today," and for "the past three minutes."

The POMS offers a broader range of state measures for the subjective assessment of stress when compared with the STAI, the AACL–MAACL, and the SSS. A more recent revision of the POMS, the Profile of Mood States Second Edition (POMS 2) is also available.

Connor Davidson Resilience Measure

The Connor Davidson Resilience Measure (CD-RISC) (Connor & Davidson, 2003) is a rating scale that assesses resilience. It is composed of 25 items that are rated on a scale of 1–4. Higher scores indicate greater resilience. More recently, a 10-item version has emerged (Burns & Anstey, 2010). There has even emerged a 2-item version (Vaishnavi, Connor, & Davidson, 2007). The two items from the CD-RISC utilized in the two item version are 1 ("Able to adapt to change") and 8 ("Tend to bounce back after illness or hardship").

Inventory of Complicated Grief Scale

The Inventory of Complicated Grief Scale (Prigerson et al., 1995) is a scale designed to assess symptoms of complicated grief. This scale is designed to assess the complicated bereavement symptoms of depression and anxiety that predict long-term functional impairments. The scale consists of 22 items corresponding to the cognitive, emotional, and behavioral states that are associated with complicated grief. Each of the items is rated on a scale of 1–4, depending on how frequently they experience each of the states.

Generalized Anxiety Disorder Questionnaire

The Generalized Anxiety Disorder Questionnaire (GADQ-IV) (Newman et al., 2002) is a self-report questionnaire that has items that are reflective of the *DSM-IV*'s (APA, 1994) criteria for generalized anxiety disorder. Most of the items are dichotomous and ask the respondent to give yes/no answers, one item is left open ended and two items utilize a rating scale from one (meaning no distress) to eight (meaning severe distress) to assess distress and impairment.

Beck Anxiety Inventory

The Beck Anxiety Inventory (BAI) (Beck & Steer, 1990) is a widely used 21-item self-report symptom inventory that is used to assess anxiety in adolescents and adults. The items reflect symptoms of anxiety and the respondents are asked to rate them on a scale of 0 (not experiencing symptoms at all) to 3 (severe symptoms). This can be used as a screening or diagnostic tool for generalized anxiety disorder. It can also be used to assess treatment progress.

Symptom Checklist-90 Revised

The Symptoms Checklist 90 (SCL-90-R) (Derogatis, 1994) is a self-report measure assessing symptoms of psychopathology on nine different dimensions and three global indices. The dimensions include anxiety, obsessive-compulsive disorder, phobic anxiety, and paranoid ideation. The SCL-90 consists of 90 items and takes approximately 12–15 min to administer. There is also a shorter form called the Brief Symptom Inventory (BSI; Derogatis, 1993) that is composed of 53 items and provides scores on the same dimensions and global indices as the SCL-90. These tools can both be used to determine treatment progress or treatment outcome.

Screen for Posttraumatic Stress Symptoms

The Screen for Posttraumatic Stress Symptoms (SPTSS) (Carlson, 2001) is a 17-item self-report inventory that assesses the symptoms of PTSD listed in the DSM-IV (APA, 1994). Respondents rate each of the items on an 11-point scale indicating frequency of symptoms from 0 (never) to 10 (always). This is recommended for screening of PTSD in both research and clinical settings.

Inventory of Psychosocial Functioning

The Inventory of Psychosocial Functioning is an 87-item self-report measure that assesses functional impairment experienced by active-duty service members and veterans over the past 30 days on a 7-point scale ranging from 1 (*never*) to 7 (*always*). The IPF provides a total score for each of seven subscales (romantic relationships with a spouse or partner, family relationships, work, friendships and socializing, parenting, education, and day-to-day functioning), and an overall functional impairment score is computed by calculating the mean of the scores for each completed subscale. In a sample of veterans meeting diagnostic criteria for PTSD, their overall mean score on the IPF was 3.86 (SD = 1.06) (Castro, Hayes, & Keane, 2011).

The Assessment of Coping

The Millon Behavioral Health Inventory (MBHI) (Millon, Green, & Meagher, 1982) assesses the patient's characterological coping style. The Hassles Scale measures an indirect form of coping within its "uplifts" subscale. Everly created a simple coping inventory for use in conjunction with the National Health Fair (Everly, 1979; Girdano & Everly, 1986). This checklist can be found in Appendix H.

The MBHI was replaced by the Millon Behavioral Health Diagnostic (MBMD) in 2001. The MBMD (Millon, Millon, & Grossman, 2015) provides an assessment of psychosocial factors that may support or interfere with a patient's medical treatment. Psychosocial factors have been identified as playing an important role in medical treatment outcome (Antoni & Millon, 2014; Lattie, Antoni, Millon, Kamp, & Walker, 2013). It consists of 165 true/false items and take about 20 min to complete. The MBMD consists of five major sections:

- 1. Response Patterns that serve to gauge response distortions and tendencies in the patient's self-report.
- 2. Negative Health Habits which identify recent or current problematic behaviors affecting health, such as Alcohol, Drug, Eating, Caffeine, Inactivity, and Smoking.

- 3. Psychiatric Indications which identify psychiatric comorbidities that may affect health care and treatment formulation. They include Anxiety-Tension, Depression, Cognitive Dysfunction, Emotional Lability, and Guardedness.
- 4. Coping Styles represent the enduring personality-based approaches to handling everyday as well as major life stressors. In addition these factors affect the patient's response to medical conditions and as such are important to understand for reasons of maximizing compliance.
- 5. Stress Moderators help identify attitudes and resources that may affect health care. They include factors such as Illness Apprehension, Social Isolation, Future Pessimism, Pain Sensitivity, and Spiritual Absence.

Validation of the MBMD consists of correlation-based construct validation.

The great strength of the MBMD is that its norms are largely those of medical patients rather than psychiatric patients or respondents who are free of illness.

Finally, perhaps the most popular of the early coping indices is the Ways of Coping Checklist developed by Lazarus and Folkman (1984). This 67-item checklist that assesses an individual's preference for various styles of coping patterns (e.g., defensive coping, information seeking, problem solving) enjoys a considerable empirical foundation and can be found in their 1984 textbook on stress, appraisal, and coping.

In the broadest sense, coping may be viewed as any effort to stabilize or mitigate the aversive effects of stress. These efforts may be psychological or behavioral. The scales mentioned sample both domains.

Law of Initial Values

A final point should be made regarding the role of individual differences in the process of measurement. No two patients are exactly alike in their manifestations of the stress response. When measuring psychophysiological reactivity, or any physiological index, the clinician must understand that the patient's baseline level of functioning on any physiological variable affects any subsequent degree of activity or reactivity in that same physiological parameter. This is Wilder's Law of Initial Values (Wilder, 1950). In order to compare an individual's stress reactivity (assuming variant base-lines), a statistical correction must be made in order to assure that the correlation between baseline activity and stressful reactivity is equal to zero. Such a correction must be made in order to compare groups as well. Benjamin (1963) has written a very useful paper that addresses the necessary statistical corrections that must be made. She concludes that a covariance model must be adopted in order to correct for the law of initial values, though specific calculations will

differ when comparing groups or individuals.¹ It must be remembered that the Law of Initial Values will affect not only the measurement of stress arousal but also stress reduction.

Summary

In this chapter, we have described briefly some of the most commonly used methods of measuring the effects of the stress response. The methods described have included physiological and psychological criteria.

The most important question surrounding the measurement of the stress response is "How do you select the most appropriate measurement criterion?" The answer to this question is in no way clear-cut. Generally speaking, to begin with you should consider the state versus trait measurement criterion issue. Basically, state criteria should be used to measure immediate and/or short-lived phenomena. Trait criteria should be used to measure phenomena that take a longer term to manifest themselves and/or have greater stability and duration. The psychological criteria discussed in this chapter are fairly straightforward as to their state or trait nature. The physiological criteria are somewhat less clear. Some physiological criteria possess both state and trait characteristics. Furthermore, normal values for blood and urinary stress indicators may vary somewhat from laboratory to laboratory. Therefore, the clinician should familiarize him- or herself with the laboratory's standard values. Before using physiological measurement criteria in the assessment of the stress response, the reader who has no background in physiology would benefit from consulting any useful physiology or psychophysiology text (see, e.g., Everly & Sobelman, 1987; Greenfield & Sternbach, 1972; Levi, 1975; Selve, 1976; Stern, Ray, & Davis, 1980). Finally, because no two patients are alike in their response to stressors, the clinician might consider measuring multiple and diverse response mechanisms (or stress axes) in order to increase the sensitivity of any given assessment procedure designed to measure the stress response (see Fig. 6.1).

Having provided these closing points, let us review the major issues discussed within this chapter:

1. It has been argued that the single most important aspect of empirical investigation is the process of the *measurement* of relevant variables. This is true of investigations into the nature of human stress as well.

therefore consistent with Benjamin's recommendation, is expressed as ALS = $50 + 10 \left| \frac{y_z - x_{zxy}}{(1 - r^{2y/5})} \right|^{2y_z - x_{zxy}}$

¹One useful formula for correcting for the Law of Initial Values when comparing individuals is the Autonomic Lability Score (ALS; Lacey & Lacey, 1962). The ALS, a form of covariance and

where X_z = client's standardized pre-stressor autonomic level, Y_z = client's standardized poststressor autonomic level, and r_{xy} = correlation for sample between pre- and poststressor levels.

- 2. The Social Readjustment Rating Scale (Holmes & Rahe, 1967), the Life Experiences Survey (Sarason et al., 1978), and the Hassles Scale (Kanner et al., 1981) are all self-report inventories that assess the patient's exposure to critical "life events." Collectively, these scales do not measure stress; rather, they assess the patient's exposure to stressors. Stressor scales are correlated with stress arousal because the physiology of adaptation to novel or challenging stimuli is also the physiology of the stress response.
- 3. The Derogatis Stress Scale (Derogatis, 1980) and the Millon Behavioral Health Inventory and Millon Behavioral Medicine Diagnostic (Millon et al., 1982; Millon, Antoni, Millon, Minor, & Grossman, 2006) represent scales designed to assess the patient's cognitive-affective status. The stress response is thus assessed indirectly through the measurement of cognitive-affective states known to be highly associated with stress arousal. It has been argued that such assessments may well be the most efficient, practical, and cost-effective way of assessing stress arousal. All of these scales also include symptom indices.
- 4. Albeit an important clinical phenomenon, the assessment of propensities for limbic efferent discharge (limbic hypersensitivity phenomenon) is extremely difficult. Subcortical electroencephalography is a crude measure at best. Electrodermal and general psychophysiological reactivity may be the best options currently available for the assessment of neurological triggering mechanisms of the human stress response.
- 5. Numerous measurement options exist for the assessment of the physiological stress response itself (if deemed appropriate).
 - (a) The neural stress axes may be assessed via electrodermal measures, electromyographic measures, as well as cardiovascular measures (heart rate, peripheral blood flow, blood pressures).
 - (b) The neuroendocrine stress axis can be measured via the assessment adrenal medullary catecholamines.
 - (c) The assessment of the endocrine stress axes is most commonly conducted via the assessment of cortisol.
- 6. The assessment of target-organ effects of pathogenic stress arousal can be conducted via standard physical medicine examination or the use of self-report inventories such as the Seriousness of Illness Rating Scale (Wyler et al., 1968) to measure *physical effects*. *Psychological effects* may be assessed via self-report scales such as the MMPI, the MCMI, the 16-PF, IES-R, SAS4, PENN, SASRQ, CGO, the TAS, the STAI, the AACL, the SSS, and the POMS.
- Coping is an important potential mediating variable. It may be assessed via the MBHI/MBMD; the Hassles Scale, a coping scale developed by Everly (1979) for the US Public Health Service; or the Ways of Coping Checklist (Lazarus & Folkman, 1984).

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