Myron A. Hofer

THE PRINCIPLES OF AUTONOMIC FUNCTION IN THE LIFE OF MAN AND ANIMALS

American Handbook of Psychiatry

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Myron A. Hofer

e-Book 2015 International Psychotherapy Institute

From *American Handbook of Psychiatry: Volume 4* edited by Silvano Arieti, Morton F. Reiser

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Introduction

When Galen described the anatomy of the visceral neural network 1800 years ago, he was led to conclude that this structure functioned to promote "sympathy" or communication and harmony between internal organs. Although the use of the word "autonomic" nervous system dates from a mere seventy-five years ago, parts of Galen's hypothesis regarding its function have survived, and the word "sympathetic" is used to denote the thoracolumbar portion of the system.

The modern literature on autonomic psychophysiology is immense and I will not attempt to survey the field; the reader is referred to recent books and review articles for this purpose (See references). Rather this chapter will deal with a few studies selected to illustrate the *principles* which appear to govern autonomic-nervous-system (ANS) functions in the organism during its natural life. The concepts which arise from new data will be emphasized, and will be related to disease processes. Emphasis will be placed on interpretation, on clinical implications, and on future directions, in this way hoping to represent the current state of our understanding of the field.

The previous chapter has dealt with the organization of the ANS at the

level of its peripheral and central mechanisms, and reviewed the contribution of laboratory studies to our understanding. This chapter will consider the properties of the ANS as it functions while the organism interacts with its environment. What are the characteristics of its functioning while the subject is at rest, in response to changes in the environment and as a part of emotional and behavioral responses to signals processed by the central nervous system (CNS)? Is the system organized differently at different developmental stages? Is it primarily an effector system or are there major roles for its afferent pathways? Does activity of the autonomic system show effects of learning as does the musculoskeletal system, and to what extent do the systems differ? Finally, what processes may account for the appearance of the unusually intense or poorly coordinated responses which can produce lasting damage or even death?

Our understanding of the role of the ANS in the economy of the organism was greatly advanced by Claude Bernard and W. B. Cannon, whose elegant experiments led them to an understanding of the negative feedback properties of autonomic function which served to maintain relative constancy of the “milieu interieur,” or “homeostasis,” in the face of constantly varying environmental conditions. It has since been recognized that such control systems are a general property of biological organization and are present in endocrine, metabolic, and cellular systems in the human." They are also thought to be a characteristic of central neural functioning, mediating

conscious experience. Since the time of Cannon, accumulating data has forced modification in our concept of homeostasis to account for the fact that hierarchies are established in the organization of central integration, so that certain functional levels may be maintained at the expense of homeostasis in another area or system. An example of this is the maintenance of temperature regulation at the expense of water and electrolyte balance during extreme heat. Observations such as these have led to the concept of variable set points and a servomechanism model. That is, the central nervous system, under certain conditions, can raise or lower the level of function in a given system toward which adjustments are made. It is in this way that central neural states may act to modify autonomic regulation.

The complex interplay of neural, endocrine, and cellular metabolic processes outlined in the previous chapter illuminates the multiple determinants of level of autonomic function and has important consequences for further understanding. The first is that any given function controlled by the ANS, for example, heart rate, can only approximate a steady state and in reality is subject to a constantly fluctuating interplay of feedback from numerous other systems such as carotid baroreceptors, pulmonary tension receptors, gastric mechanoreceptors, etc., as well as being affected by many systems outside the ANS. The second consequence is that a given change in level of any one autonomic effector system can be produced by one of several different mechanisms. A rise in heart rate, for example, may be produced by a

decrease in vagal tone secondary to subsidence of a gastric contraction, or by an increase in sympathetic tone following baroreceptor stimulation, occasioned by a fall in blood pressure due to pooling of extracellular fluid in the legs while sitting down after walking; the list can go on and on. The third consequence of this multiple servocontrol organization is that the response (to a standard environmental stimulus) in any given ANS effector function is greatly affected in degree and even in direction by the current status of continuing and reverberating homeostatic adjustments in other parts of the system as they play back upon the given response system.

These consequences create an extraordinary range of possible variability in autonomic effector function under natural conditions. There is a considerable degree of unpredictability even between observations of steady states and in response to even the most discrete and definable stimulation. The variability is large both within the individual from one point in time to the next and between individuals at any given time.

Some of the sources of variability can be minimized by the controls which are possible in clinical laboratory investigation. However, very few studies have been done with the highly desirable control, for example, of extracellular fluid volume, which so affects cardiovascular regulation and then indirectly many other functions. Diet, temperature, humidity, and the activity of human experimental subjects, are arduous controls when they

must be maintained for days prior to an experiment.

If this were the extent of the interactions at work in the functional control of the ANS, this section of the chapter would be shorter but less interesting. There are, in addition to the homeostatic feedback characteristics of the system, two major forms of servomechanism "override" exerted by the CNS. The first of these are the regular, time-related processes of circadian rhythms and of developmental changes. The second involve the irregularly occurring events in response to which the balanced homeostatic organization is overridden by central neural activity, apparently of higher priority, for example, by responding to symbolic environmental stimuli, such as a signal that an athletic contest is about to begin, before the physiological demands of the event itself.

Man at Rest

No studies have been performed in which all or most of the interconnected systems of the ANS described above have been measured simultaneously in man even under basal conditions. Therefore, no complete picture is available of the patterned functioning of the ANS. A few investigators have been aware of the necessity of studying the *pattern* of levels of functioning and have emphasized the importance of the relationship of the level of activity in one function to that in another.

Sargent and Weinman, in an intensive study of army recruits, simultaneously measured more than thirty physiological variables, half of them directly reflecting autonomic neural activity and the others involving water, electrolyte, and nutritional metabolic systems.

Repeated measurements were made at intervals over several-week periods and repeated at a different season of the year. Because the subjects were in the Army, they were under unusual control by the experimenters, so that such factors as diet and activity could be strictly prescribed throughout the experiments. The most striking finding in the observations made at rest was the great individuality of the patterns exhibited by each subject. Like fingerprints, the relationship of one autonomic effector system to another was very different in one individual than in another. There seemed to be no one characteristic pattern for the group. In the observations made on the same individuals at a different season of the year (six months later), the individual patterns had changed. Moreover, there did not seem to be any regularity in the kinds of changes in the individual patterns.

The complex nature of the interrelationships between component parts of the ANS, the extreme individuality of the patterns of ANS activity observed between individuals in the resting state at one point in time, and the inconstancy of a given pattern in the same individual with time (despite rigorous efforts to reproduce an identical resting state) are all fundamental

characteristics of ANS organization.

These and other data are consistent with the conceptual scheme outlined in the Introduction, in which multiple feedback relationships between the widespread organ systems innervated determine a complex pattern of balance, subject to a host of environmental factors as well as to individual differences in relative set points. How certain environmental, internal biological, and psychological processes come to exert predictable control over this organization will be the focus of this chapter.

Circadian and Other Rhythms

So far we have examined the functioning of the ANS only in the resting state and only at a single point in time. Repeated observations in man over a period of days disclose pronounced regular, rhythmic fluctuations in all autonomic functions studied. The previous chapter has described some of the transduction mechanisms for altered neurotransmitter and enzyme levels. Although individuals show slight differences in the timing and scope of these fluctuations, everyone has daily high and low points in levels of functions, many of these independent of environmental lighting, activity, posture, and even of sleep. The low points generally occur during the time of darkness, and the high points soon after dawn and awakening, although there are many exceptions to this generalization.

Although these rhythms can be synchronized by such natural rhythmic environmental events as light and temperature change, and can be caused to cycle at slightly more or less than an exact twenty-four-hour period, they retain their rhythmic behavior in the absence of external cues, thus indicating the existence of an internal "clock" with rhythmic oscillations in set points of ANS function. After prolonged deprivation of all usual daily cues (e.g., isolation in a cave)66 circadian rhythms become desynchronized, each running at its own period, either slightly more or slightly less than twenty-four hours in length, creating a steadily changing pattern of relationships between individual functions.

Cyclic fluctuations of a shorter period, often approximating ninety minutes in duration, have also been described for some functions and are termed ultradian. More familiar are the annual, seasonal, and monthly rhythms. Autonomic balance has been shown to alter in a rhythmic fashion in time with the human menstrual cycle.

Developmental Changes

Circadian rhythms in autonomic function are not present at birth in the human, with the exception of skin resistance. Most physiological functions studied show an ultradian rhythm throughout the first postnatal months. Heart rate becomes circadian in rhythmicity at four to twenty weeks but body

temperature requires twenty to forty weeks. The factors affecting the rate and regularity of development of these rhythms in early life is an area of current study. Both the inanimate and the social environment of the baby during this early period have been shown to affect maturation of rhythmic behavior.

In addition to the ultradian, circadian, and seasonal rhythms, the span of an individual's life exerts its own temporal patterning on ANS functioning. Such levels of ANS functioning as heart rate and blood pressure are known to vary systematically with age in man. Blood pressure rises with each decade from birth onward. Resting-heart rate increases after birth during the first few months, is maintained at relatively high rates in childhood, then shows a pronounced decline, reaching a low plateau in adolescence, and rising again slightly throughout adulthood. The pattern is very similar for at least one animal species, the rat, in which it is possible to determine some of the factors involved, Adolph has shown that the rat heart responds to neurotransmitters from late stages in fetal life, and that developmental changes are neurally mediated and not due to maturational changes in the myocardium itself. Hofer's work has demonstrated that the high rates during late infancy are the result of high sympathetic tone and that this is, in turn, supported by the mother through her milk which appears to act via a neural mechanism involving the CNS. The subsequent decline of heart rate in late childhood in both rat and man is the result of increasing vagal tone, which had not been

present earlier.

The existence of distinctly different patterns of autonomic organization at different developmental stages and the interactions of environmental and social factors in the development of adult patterns are areas with much promise for future study (see below).

Autonomic Responses

We have developed a picture of the ANS in man at rest under basal conditions as a dynamic system organized to maintain certain levels of function by an elaborate network of checks and balances. These levels of function, in turn, vary in a highly systematic rhythmic fashion around each twenty-four-hour period, programmed by an internal clock which is synchronized ("entrained") by certain daily recurring environmental events. The multiple interconnected feedback relationships described above and in the preceding chapter may alter the intensity and even the direction of a response to a given stimulus, depending on the status of these systems at the time of stimulation. Partly as a result of these interactions, the resting or prestimulus level in a single autonomic effector system can only be a rough predictor of response according to the "initial value" effect. (By this empirical rule, response magnitude should be inversely related to initial resting level.)

As indicated above, in evaluating autonomic responses in man we must

distinguish between (1) nonspecific or spontaneous activity bursts; (2) the final level of function attained during the response; and (3) the magnitude of change in level as a result of the response. Lacey has emphasized that these parameters must be considered independently. He has also shown that responses in different autonomic functions (e.g., heart rate, skin resistance or blood pressure) to the same stimulus have a low correlation. As a result, *patterns* of responses will be more meaningfully related to stimuli than single variables. Nevertheless it is worth pointing out that a *general* relationship can be demonstrated to exist between measures of intensity of physical stimulation (e.g., touch or noise) and magnitude of response in autonomic variables (e.g., skin conductance, heart rate, or finger volume). This simple quantitative principle operates in addition to a number of more complex qualitative determinants of direction and intensity of response which will be discussed later in the chapter.

The autonomic system is organized to respond to a large variety of environmental events in which the organism participates. These will be discussed below, beginning with the simplest and leading to the complexity of elicited emotional states.

Orienting Responses

A fairly uniform pattern of altered ANS activity follows a novel and

unexpected change in the environment. For example, a sudden sound, even a weak one, or a sudden reduction in an ongoing level of sound, elicits cortical alerting with characteristic EEG and evoked potential changes, accompanied by a sudden increase in skin conductance, a fall in heart rate and in both systolic and diastolic blood pressure, vasoconstriction in the extremities and vasodilation in external cerebral vessels. This response pattern becomes progressively less intense and finally disappears if the same stimulus is repeated several times (habituation), but may at any time be elicited again by a qualitatively different stimulus, for example, a tone of a different pitch.

If the stimulus which initially elicits an orienting response is repeatedly followed by a task which the subject is motivated to perform, it continues to elicit the same ANS pattern and fails to habituate. The stimulus now has "signal properties," continues to arouse attention, and may also arouse some ANS preparatory adjustments appropriate to the task which is about to be performed, e.g., tachycardia before exercise. The ANS pattern thus becomes modified through a process of conditioning (see below, under Autonomic Learning).

The Laceys have studied the relationship between the heart-rate deceleration observed in response to a signal for a reaction-time test and the subject's performance on the test. They have found data to support the hypothesis that the ANS adjustments of the orienting response serve the

purpose of increasing cortical vigilance via ANS afferent feedback to the CNS (see below under Afferent Influences.)

It is apparent that even such a relatively simple psychophysiological human response is in fact a pattern of great complexity. Real understanding of its nature is a formidable analytic task. At present the barest descriptive outline of the full pattern is possible.

Defense Responses

With more intense stimuli, the orienting response is discernible only during the initial portion of the subject's response to the first such stimulus presented, and is rapidly overtaken by another pattern, the defense response. Some of the physiological characteristics of the orienting response are retained, (e.g., EEG activation, increased skin conductance and peripheral vasoconstriction) in a prolonged and intensified form. Other autonomic functions change in the opposite direction: heart rate and blood pressure are generally increased and external cerebral blood vessels are constricted. Muscle tone and respiratory frequency and amplitude are usually increased in the moments following stimulation at near painful intensity. These patterns and appropriate behavior have been elicited by brain-stimulation studies as described in the preceding chapter. Another characteristic of defense responses is that they do not cease to occur after the first one or two

repetitions of the stimulus (habituation) as do orienting responses. They do undergo a complex series of changes in patterning with repetition, although little systematic data are available on this point.

It is worth noting that the behavior of the organism is quite different in response to weak as compared to strong stimuli (provided these stimuli have not acquired special signal properties). Weak stimuli generally elicit a turning of gaze and posture toward the stimulus and often result in approach of the organism to the stimulus, associated with conscious experience which may be described as curiosity or attention. Strong stimuli generally elicit withdrawal or even generalized escape movements, movement away from the stimulus and the experience of pain and fear.

There is evidence that some of the autonomic correlates of the defense response (e.g., increases in heart rate and blood pressure) may activate afferent ANS pathways serving to reduce cortical excitability and diminish or attenuate the impact of the stimulus upon the CNS (see below under Afferent Influences).

The autonomic responses cited may also be viewed as preparatory mobilization of some of the characteristic physiological changes of physical exertion, preparing the animal for fight or flight. Increased survival capability of animals so prepared has presumably resulted in a selective process

favoring this form of ANS organization during evolution.

Exertion

We move now to a consideration of the functional organization of the ANS during physical and mental activity which is sustained and organized over a period of time. For many years, the alterations in cardiovascular dynamics during exercise were explained as proceeding from increased venous return due to the pumping action of active skeletal and respiratory muscles and to vasodilation in muscle beds produced by the local accumulation of metabolites. Hemodynamic principles discovered in isolated heart-lung preparation were freely applied in unchanged form to the intact, unanesthetized animal. The role of the ANS was thought to be entirely reflexive, as in the Bainbridge reflex, whereby the increased cardiac rate during exercise, although mediated by sympathetic nerves, was thought to be reflexively dependent on increased venous filling.

Rushmer and Smith have summarized the large body of evidence which reinstates the CNS and its autonomic cardiovascular connections as prime movers in the cardiovascular as well as the behavioral patterns of exercise. Some aspects of their work have been described in the previous chapter. Central to this chapter is their finding that the cardiovascular changes characteristic of physical exercise in the dog could be elicited either by

anticipation of treadmill exercise or by brain stimulation under anesthesia, despite the fact that in these two situations no exercise occurred. Thus, although the behavior and the characteristic ANS cardiovascular adjustment pattern ordinarily occurred together and appeared to share common central neural pathways, either could occur without the other. This demonstration of the dissociability of behavioral and physiological events in the simple situation of treadmill exercise illustrates a fundamental principle of ANS function and of how it is organized in relation to behavior (and conscious experience) which I will return to repeatedly in the subsequent sections.

The autonomic control of regional vascular tone, and of cardiac rate and force of contraction during physical exertion, is brought into play with almost exactly the same pattern of changes during the performance of *mental* tasks such as mental arithmetic. Brod's now classic studies show that the most frequent pattern during serial subtractions was one of increased cardiac rate and output, with a fall in total vascular resistance despite vasoconstriction in skin and renal vascular beds. Muscle beds, such as the forearm, showed increased flow and thus decreased vascular resistance. Blood pressure, both systolic and diastolic, rose slightly.

These studies by Brod and Rushmer and Smith, and others employing simultaneous measures of cardiac output and regional blood flow, permit calculations of changes in vascular resistance by regions, and give a far more

complete understanding of ANS functioning than the usual psychophysiological studies. For example, as Brod's studies show, two subjects with similar increases in blood pressure may nevertheless differ remarkably in the balance between cardiac output and total peripheral resistance. He was able to define a second pattern, occurring in a minority of subjects in whom cardiac output actually fell during mental arithmetic. In these people (four of eighteen studied), total peripheral resistance consistently increased and this could be attributed to increases in extrarenal vascular resistance exclusive of the muscular (forearm) vascular bed. All subjects showed increases in blood pressure, so that Brod's differentiation of subjects into "output" and "resistance" types would have been impossible without the multiple simultaneous measures.

Brod states that the test provoked "emotional stress," and gives as evidence that "subjects blushed, became tense and nervous and made frequent mistakes which caused them great embarrassment." Thus, even in this very standardized task situation the subjects' emotional response became a major (uncontrolled) variable. One wonders whether the "output" and "resistance" types of ANS pattern could have been differentiated in terms of the emotions present while performing the task. The work of Funkenstein and Wolf et al. in the 1950s suggests, on the basis of the very indirect cardiovascular measures then available, that those who suppress hostility and do not express their anger at the experimenters directly, give rise to the

"resistance" type of pattern. The vital importance of the relationship of the subject to the experimenter will be considered further below.

Appetitive Behavior

Since the process of digestion is complex and the autonomic physiology involved is adequately covered in standard physiology texts I will only mention that a highly reproducible pattern of changes in motility, secretion, and blood flow are set in motion by the ANS in response to digested food. The degree of higher neural control over this process is illustrated by the anticipatory changes in salivary secretion, gastric motility, and heart rate, occasioned by signals prior to the appearance of the food itself and mediated by ANS activity.

Sexual behavior is characterized by many responses organized through the ANS, the central neural pathways which have been described in the previous chapter. Some of these are similar to those occurring with any exertion (greatly increased pulse and blood pressure) but many are quite specific. There appears to be a shift of blood flow to the skin rather than away from it as in ordinary exercise, and local vascular engorgement (e.g., lips, ear lobes, nipples, and genitalia) is pronounced and unique to this form of stimulation. Profound alteration in sweat and specialized glandular secretion, and patterned changes in respiratory depth and rate, are also mediated over

autonomic pathways. The regular course of development of these changes throughout an episode of sexual intercourse for both male and female has been described by Masters and Johnson, as well as the variations in timing and stages which occur. Despite the lack of sophisticated physiological instrumentation, their observations have made clear the general outlines of these patterned responses and opened up an area which had previously never been studied systematically.

Special Situations

There are a number of additional life situations, less commonly encountered than those previously described, which evoke pronounced autonomic changes. These have been amply reviewed. Many of them may be considered to be primarily physical stressors, such as heat, cold, and centrifugal acceleration, but also arouse emotional responses and other psychological processes which participate in the final autonomic response patterns. Since many of the responses are quite similar to the defense and exertional responses already described, I will deal with others which exemplify a different sort of autonomic pattern, one in which marked *decreases* in cardiac output and other adjustments occur which appear to serve the function of conserving rather than mobilizing the resources of the individual. Brain sites have been identified which give rise to behavioral and autonomic patterns on stimulation which bear some resemblance to this class

of responses.

The most clear-cut example of this kind of response is the dive reflex. Present in most mammals, this sudden and profound cardiovascular adaptation occurs most clearly in sea mammals such as the seal, but also in diving birds such as the duck. It has recently been studied in man and in dogs by Eisner. When a man immerses his face in water, while holding his breath, an immediate and profound vagal bradycardia occurs. Eisner recorded one healthy young man who sustained an eighteen-second period of asystole. This cardiac rate change is part of a complex pattern of readjustments. There is massive peripheral vasoconstriction which shunts blood away from all areas capable of anaerobic metabolism, such as muscle and the splanchnic area, thus preserving blood oxygen stores for brain and myocardium. The cardiac output accomodates to a much smaller functioning vascular bed by decreasing markedly. Sensory stimuli capable of eliciting this response include both tactile activation in the distribution of the trigeminal nerve, and the pulmonary afferent stimulation involved in sudden breath holding. Anoxia does not develop in time to play a role in these immediate responses. Metabolic adjustments taking place during prolonged dives have been reviewed by Andersen.

Forced—as contrasted with spontaneous— dives in seals have been reported to elicit episodes of atrial fibrillation and ventricular tachycardia

and Wolf has suggested that some cases of unexplained sudden death in adult and infant humans may involve the mechanism of the dive reflex.

A response which is less consistent among individuals, but which can be elicited by a variety of stimuli is fainting or "vasovagal syncope." Typically, the early phases of this response are characterized by piloerection, dilation of the pupils, cardiac acceleration, and decreased blood flow to the skin and viscera. However, blood flow to the muscles is increased greatly. (This vascular response is a critical element and can be largely blocked by intra-arterial atropine, indicating the role played by cholinergic sympathetic vasodilator fibers.) A fall in systemic vascular resistance occurs, accompanied by a decrease in cardiac output rather than a compensatory increase. Blood pressure falls, systolic before diastolic, and finally a vagal bradycardia occurs. If the subject is erect, brain blood flow is seriously compromised and he loses consciousness. The slowing of the heart is not a necessary part of the phenomenon and syncope can occur without it. Muscular inaction may play a necessary role in the development of the condition, since the fall in cardiac output is partially due to lack of venous return from the muscular venous pump.

A lack of ANS support for cardiac output in the face of decreased peripheral resistance and muscle-bed vasodilation is the basic pattern of ANS organization in this form of syncope. The stimulus situation which most

regularly provokes this ANS response is blood loss, and occurs in experienced blood donors after 15-20 percent of blood volume is removed. Pooling of blood and loss of effective blood volume by filtration of plasma into dependent limbs during prolonged maintenance of the standing position can lead to syncope, as it may occur on the parade ground. Cutaneous vasodilation in a hot environment is an ANS response which predisposes to the development of this more complex ANS response. Most interestingly, syncope may be provoked by apparently trivial stimuli which have signal properties (e.g., the sight of blood), or sometimes in association with physical pain.

The response appears to be one in which musculoskeletal inaction is superimposed upon peripheral ANS responses appropriate to vigorous exertion. This in itself does not explain the fall in cardiac output or the bradycardia. Graham emphasizes a sudden cessation of the hyperdynamic state, and has found a subjective sense of relief just before syncope as, for example, when an injection has been completed and the needle is withdrawn. Engel has evidence from other situations which point to a cognitive and emotional state of helplessness and "giving up" which immediately precedes the syncopal episode.

Altered Central States

The relationship of central neural states to the functional organization of the ANS is poorly understood. Only emotional states have received much study, although they are vastly more difficult to reproduce and subject to numerous methodological complications. As a result, they will be considered in a separate section. Recent work on the state of sleep has made it clear that the ANS is organized very differently during sleep and even according to the subdivisions (stages) of the state of sleep. The fact that ANS response characteristics can differ substantially according to changes in central neural state has clear implications for our understanding of how the ANS operates in the complex situations developing in natural life when emotions, physical activity, sleep, mental tasks, cognitive processes, and psychological defenses are all operating together.

Sleep

Rapid "flurries" of changes in respiratory rate, blood pressure, finger blood flow and heart rate occur in close association with rapid eye movements during stage "REM sleep." In addition, it has recently been shown that flurries of spontaneous fluctuations in skin resistance—"GSR (galvanic skin response) storms," occur predominantly in Stage 4, slow-wave sleep. Heart-rate responses to an auditory stimulus (see Orienting Responses, p. 532) are found to be *more* pronounced and to have markedly different shape and latency during Stage 2 and Stage REM than when the subject was awake

or in Stage 3-4 of sleep. Furthermore, there was no habituation of the heart-rate response as long as the subject remained asleep! Another important difference involves the thresholds for activation of responses in relation to the threshold of arousal. In Stage 2, the EEG response (k-complex) first appeared to tones 30 decibels (db.) below that required for arousal from sleep. The finger-pulse response occurred 15 db. below arousal threshold, the heart-rate response at 5 db., and the electrodermal response did not occur until the subject was aroused from sleep sufficiently to show an awake EEG and made a motor response.

These findings argue definitively against any concept of ANS function as operating on a simple arousal continuum from low levels of function during basal states in sleep to the highest levels during the heights of arousal in response to maximal stimulation. Rather, the functional organization seems to be reprogrammed during shifts in central neural state, so that specific response characteristics, spontaneous activity levels, and thresholds are all altered in a highly complex manner. Even such fundamental a characteristic as habituation can be suspended during certain stages of sleep.

During the flurries of autonomic activity and inhibition in REM sleep, patients with borderline cardiovascular adjustment may enter frank pulmonary edema or life-threatening cardiac arrhythmia. It is out of slow-wave sleep that classic night terrors arise. In these, profuse sweating and

violent tachycardia have been noted, indicating intense autonomic activation. Mental content is usually fragmentary and indistinct, although intense anxiety is usually described. In contrast, ordinary anxiety dreams occurring during REM sleep may involve exceedingly vivid and specific hallucinatory experiences, also with intense affects aroused, but this intense emotional activation may occur *without* any alteration in autonomic variables recorded at the time of the dream. Autonomic flurries are more regularly associated with periodic REM than with dream content.

These observations raise an extremely important point to be kept in mind throughout the remainder of this section. The ANS is not organized so that there is any *necessary* relationship between feeling state and levels of autonomic activation. Emotions, or indeed any consciously recognized states, are not causally related to changes in the ANS and indeed the two are not necessarily associated. Both conscious state and autonomic activity can vary independently. It is this generally unrecognized fact which helps to explain why efforts to use the measurement of autonomic variables as indicators of mental state have generally been unsatisfactory or difficult to reproduce. In the example given, the state of sleep appears to act to dissociate the emotions from the autonomic responses. Our knowledge of how this is accomplished is fragmentary but we know that other conditions may have the same effect during other states. Research needs to be redirected toward analysis of the processes responsible for full or partial dissociation between feeling state and

ANS activity.

Transcendental Meditation

Wallace and co-workers have obtained data on ANS function during a relatively simple form of focused attention (transcendental meditation) and have revealed a hypometabolic state with markedly decreased oxygen consumption, decline in blood lactate, respiratory rate, and heart rate while skin resistance markedly increased. Blood pressure remained unchanged. The EEG showed increased quantity and amplitude of slow alpha rhythm at 8-9 hz. These changes were compared with changes in a few subjects who were hypnotized or asleep; the oxygen consumption, in particular, was reduced far more swiftly and more dramatically during meditation than during either of the other altered CNS states.

Little systematic work has been done on ANS organization during induced alterations of consciousness and this appears to be a fertile area for future work.

Emotion

I have reviewed in some detail the organization of ANS function in a variety of relatively well-defined conditions and in response to relatively simple stimuli, in order to provide a base from which to move on to the welter

of data which has been collected on ANS function in emotional states. If we view emotions as consisting of altered central states which interact with numerous other processes (described in other sections of this chapter) in determining autonomic response patterns, we will avoid much of the difficulty which has beset the area of the autonomic nervous system and emotion.

One of the major difficulties experienced by investigators in this area has been in collecting and adequately describing the psychological data with which they sought to correlate their physiological measurements. In fact, for a time, some seemed to be attempting to describe and even quantify emotional states *in terms of* measurements of ANS function. Other investigators, convinced by the results of such attempts that this was the wrong approach, adopted the position that qualitative differences in emotional state were of little importance, but that degree of arousal determined the intensity of a general ANS activation pattern consisting of heightened sympathetic activity in all portions of the system. This position is still held by many workers despite the considerable body of evidence which has accumulated against a simple arousal model, some of it described above. Finally, much of the data collected in experimental situations fails to take into account such facts as the importance of the subject's preconceived ideas about the experiment and his relationship with the experimenters themselves. These variables have repeatedly been shown to have a determining effect on the degree, direction,

and patterning of ANS response to the supposedly “standardized” emotional experience under study. For example, Weiner et al. demonstrated that maximal physiological responses often occur on the first exposure to the laboratory and before the procedure for inducing emotional states was begun. Then, when the subject made up a story in response to a thematic apperception test (TAT) card but did not have to tell it to the experimenter, the autonomic responses were a fraction of those observed during the verbal report of similar mental content. Thus, the subject’s autonomic responses were determined as much by his relationship with the experimenter as by the psychological stimulus being studied (TAT cards).

Studies in animals are leading to an appreciation of the highly specific autonomic patterning which is present during emotional states, and to an understanding of the processes which determine these patterns. Zanchetti has shown, for example, that whereas cats show a diffuse, prolonged, bilateral cholinergic vasodilation during immobile alerting caused by the sight of a dog, a localized, discrete cholinergic vasodilation occurs with attack movement, limited to the moving limb only. Rats subjected to brief electric shock show decreased blood pressure immediately afterwards when shocked in pairs but increases after being shocked alone.

The old view that autonomic nervous regulation is governed simply by homeostatic principles is no more erroneous than the more recent view that

autonomic responses in man are determined by emotions and can be simply correlated with affects. To be sure, situations designed to arouse one particular affect tend in general to arouse a pattern of autonomic response which can be statistically differentiated from that occurring when a different affect is provoked. However, simple tracking, tapping, or reaction-time tasks with minimal affective arousal, evoke similar autonomic patterns which likewise show a similar "situational stereotypy" as Lacey termed it. Also there are the converse findings that some subjects show minimal or no response in the autonomic systems monitored, despite the presence of affective arousal. From this evidence we must conclude that the relationship between emotional states and autonomic response patterns is far from simple. In fact, there is new evidence that the two may be predictably dissociated by manipulating the contingencies of the situation. Associations between emotional behavior and the ANS may be the result of frequent concomitance, rather than of a necessary functional relationship.

Brady studied monkeys which were anticipating electric shock during a three-minute auditory signal immediately preceding the shock. The emotional behavior studied was inhibition of a stable, previously conditioned, lever-pressing response for food reward. The physiological variables recorded were systolic and diastolic blood pressure and heart rate. Each of a series of monkeys was followed through a long series of repetitions of this basic paradigm, with variations being periodically introduced only in the

contingencies between signal and electric shock. These studies provide many examples of clear-cut alterations in autonomic patterning without concomitant detectable changes in emotional behavior. Likewise, changes in emotional behavior were observed to occur without alteration in the associated autonomic patterns. Furthermore, these experiments demonstrate how environmental contingencies affect both autonomic pattern and emotional behavior and suggest that the processes by which responses are evoked in the two systems may be functionally independent.

We thus confront again one of the central unanswered questions in ANS psychophysiology: what are the factors responsible for the maintenance and disruption of correlated functioning of emotional experience, behavior, and physiology by the CNS during life experience? Although other sections of this chapter describe functional characteristics of the ANS which bear on this question, there are several approaches dealing particularly with emotional states which should be mentioned in this section.

Psychological defenses and general coping mechanisms involving cognitive and behavioral processes intervene between stimulus and response in the human, and have been shown to modify the relationship between the situation and the affective and physiological responses. Although more work has been done on this subject in the psychoendocrine than the autonomic areas, there is ample evidence that classical intrapsychic defenses as well as

cognitive styles ("leveling-sharpening," "field independence-dependence") may modify autonomic responses as well as mental experience. These findings generally describe an interaction by which intensity of affect and of autonomic reactivity are concurrently reduced by psychological processes which tend to ward off, transform, avoid, or blunt the impact of the potentially painful experience.

Another view, based primarily on clinical observations, describes the converse relationship: the repression of affects (particularly anger) is held to result in greater autonomic responses to a situation whereas affect expression reduces the autonomic disturbance. This theory is sometimes used as a hypothesis for the etiology of some psychosomatic illness. Oken has specifically tested this notion and found little general support for it. In fact, his data slightly suggest a contrary result. Systolic blood pressure, heart rate, respiratory rate, skin resistance, and muscle-blood flow were all somewhat *more* responsive in those subjects in the high extremes of affective range and lability. The low affect group did, however, show a statistically insignificant tendency toward greater responsiveness in three measures of peripheral vasoconstriction.

The foregoing study used healthy volunteers and it has been shown that patients with an illness involving the ANS (Raynaud's Disease) were physiologically more responsive in the organ system of their illness than

healthy people. In yet another study, Weiner found that young patients with labile essential hypertension showed relatively reduced cardiovascular responses to an emotionally arousing laboratory situation. They showed reduced affective response and failed to show increased physiological responses. A few individuals were notable exceptions to this generalization. Until we can understand these and other contradictory findings, we must remain aware that there is still a great deal to be learned about the relationship between psychological functioning, affects, and autonomic responses.

For example, we generally think of the autonomic system as an effector system working on the internal environment, much as the musculoskeletal system works on the external world. Autonomic responses are thus viewed as regulatory, adaptive, or even pathogenic for *viscera.* And yet there is mounting evidence that autonomic responses may play a role in regulating *central* psychological processes and emotional states through afferent feedback. This new role for the ANS may force modification of many of our concepts regarding the role of autonomic responses and the emotions. Autonomic responses may serve to temper, modulate, and shape central emotional states.

Afferent Influences

Perhaps the most exciting and least appreciated aspect of how the ANS works involves its function in conveying information from the internal organs to the CNS. This topic has been surprisingly neglected during years of research on the ANS and it is commonplace to find autonomic pathways represented in textbooks as one-way effector pathways. It is almost as if the collapse of the James-Lange theory of emotions (that they were *caused* by visceral sensations) took with it all study of ANS afferent function. The previous chapter has outlined the anatomy and neurophysiology of these afferent pathways.

Russian work on classical conditioning involving "interoceptive signaling" has continued over the years, however, and has demonstrated that humans can make very fine discriminations among visceral sensations previously thought to be diffuse and global. For example, a water jet at one location along the small bowel mucosa can be distinguished from another several inches away, after appropriate training. Recent experience with biofeedback training suggests that information about internal states is available to the CNS, but is ordinarily appreciated only in the most vague and poorly differentiated manner. Training improves the clarity and discrimination of the internal perceptions and may provide the basis for some voluntary control over internal processes (see below under Autonomic Learning.)

A second area which has exciting potential significance for our understanding of ANS function, involves the role of afferents from cardiovascular organs in controlling central neural functions, such as attention, and perhaps in modulating affective states. The evidence for this concept has been reviewed recently by the Laceys. Neurophysiological and neuroanatomical studies have been reviewed in the previous chapter. The most impressive direct behavioral evidence for the central effects of this afferent feedback has been provided by Zanchetti and co-workers, who have shown that the behavioral syndrome of "sham" rage in the decorticate cat can be instantaneously halted by stimulating pressoreceptive afferent fibers from aortic arch or carotid sinus.

Lacey has evidence from studies with humans, using reaction-time measurements, that decreases in heart rate immediately before a task may function to improve performance. This effect is presumed to be mediated through cortical alerting via autonomic afferent pathways, the converse of the inhibitory effects observed with increases in blood pressure. Obrist has subsequently shown, however, that the decreases in chin electromyogram (EMG) and respiratory rate are equally or even more closely related to performance. His data suggest a more generalized and complex pattern of preparatory adjustments capable of altering afferent feedback to the CNS over a number of different pathways. These short-term effects, mediated over afferent neural pathways, complement and/or counterbalance long-term

effects of ANS activation operating over hormonal pathways.

These findings suggest how autonomic responses, such as increases in blood pressure, by stimulating baroreceptor nerves, may act to damp or even block central neural responses to environmental stimulation. This suggestion is a particularly interesting one because of the implications it has for psychophysiological theory. The ANS response is no longer viewed as simply deriving from or reflecting a central state but as having the function of feedback control over the central neural state. Here is more evidence that emotional behavior and autonomic responses may have to be studied as organizationally distinct subunits capable of having important interactions, rather than as components of a single integrated response pattern.

Individual Differences

In the preceding section I have described some of the organized patterns of autonomic regulation which are characteristically found during certain states, activities, and behaviors occurring in the course of natural life. The complexity of the patterns possible, the interrelationships of the various effector pathways, and their afferent feedback have already been introduced as contributing to remarkable differences between individuals in the actual ANS patterns shown under these conditions. Fortunately, we have some fundamental data to answer the following questions: To what extent are

individual differences important? Is there consistency in these differences when the individual is repeatedly observed in the same situation? To what extent is a given individual consistent in his autonomic patterning in response to different situations?

Lacey has found that the mean skin conductance and heart-rate changes of a group of college-age, male subjects during a cold pressor test can be reliably differentiated from the pattern of the group during a reaction-time test or during attention to a tape-recorded story. Differences in mean direction of heart-rate response, as well as differences in degree, characterize each situation. However, if the individual data are examined, many deviations from the mean group pattern can be found. Such individual patterns are not simply the result of random variability with time due to the action of interrelated variables such as temperature or fluid intake which may influence ANS function. Lacey has shown that individual patterns are maintained to a significant degree over intervals as long as four years and are thus consistent modes of functioning. Here again, there are exceptions, approximately one third of the subjects showing correlations between test and retest below $r = 0.30$. Finally, if test situations are not too dissimilar, correlation can be found in individual patterns across different situations, although there are notable individual exceptions. In general, individuals show a significant tendency to respond consistently in a pattern which is characteristic for them. For example, one autonomic variable may be found to

be minimally reactive to a wide variety of situations and another, maximally reactive. Interestingly there is some evidence that subjects with complaints in a given system tend to be most responsive in that system, a fact with some implication for pathological mechanism (see below). In addition, subjects who are variable instead of consistent in their individual response patterns have been studied and found to differ, for example, in cognitive style.

Thus we are faced with the fact that the ANS pattern is determined to a significant degree both by the situation and by the characteristics of the individual, as well as by uncontrolled factors productive of more random-appearing variability. The attention to individual differences has been far greater in psychophysiology than in other areas of biological study, where they are obscured by analysis which emphasizes the central tendency of large groups of subjects. The factors which correlate with these individual differences appear to be almost limitless, and yet we have only fragmentary information on the most obvious, the genetic determinants.

Most of the available genetic studies on autonomic function involve blood-pressure regulation, reviewed by Pickering. Identical twins show extremely high correlation in blood pressures from normal to hypertensive range, fraternal twins less so. Rats can be bred to be hypertensive and so, apparently, can humans, although there is disagreement as to the mode of inheritance. No studies have been done on the *extent* of interindividual

variability in blood pressure which can be accounted for by genetic determinants, for example by studying identical twins raised in separate environments. Other aspects of autonomic functioning have been more neglected, and no detailed study of autonomic response patterning in identical and fraternal twins has been done, to my knowledge. Despite this lack of real information, there is a strong tendency for genetic factors to be taken for granted as important determinants of autonomic functional organization.

Numerous investigators have attempted to understand the differences between individuals in ANS response pattern to a given situation as a function of their psychological response to the situation. Others have found that enduring characterological or cognitive differences between individuals are associated with ANS pattern differences. A focus on the transaction between the subject and the experimenter or the patient and the therapist is preferred by others, and here again significant associations can be demonstrated between these interchanges and the pattern of ANS responses.

All this evidence leaves no doubt that the regulation of ANS function is influenced by a range of neural systems serving a wide variety of affective and cognitive functions. We lack any unifying hypothesis through which these myriad influences can be logically arranged and we have no clear idea how any of these influences may become so prepotent as to cause alterations of

pathological intensity which are not compensated by homeostatic regulation. Some processes by which ANS organization can be altered or molded during life experience will be discussed below.

Plasticity of Function

Throughout the discussion thus far, individual differences in ANS functional organization have been repeatedly encountered. For the most part, these individual characteristics are relatively stable, and are thought to be an expression of the interaction between genetic and environmental determinants in the previous life history of the subject.

In recent years, two kinds of research have begun to explore the environmental contribution to the development of individual differences in ANS response, the role of autonomic learning and the effects of early experience on physiological development. Both of these kinds of environmental interactions have already been shown to have the capacity to alter psychophysiological function in consistent and systematic ways. Knowledge of these processes may help us to understand the origin of psychosomatic illness, to treat such conditions more effectively, and even to prevent their occurrence.

Autonomic Learning

The ANS, in most of its effector systems, demonstrates the three basic forms of short-term adaptation characteristic of the musculoskeletal nervous system: (1) learning not to respond (habituation); (2) learning by association (classical conditioning); and (3) learning by effect (instrumental conditioning).

The simplest and, paradoxically, the least thoroughly studied form of short-term adaptation is the phenomenon of habituation, the progressive waning of response to a repeated stimulus. I have touched on this phenomenon earlier when discussing the orienting response.

It must be distinguished from simple metabolic fatigue or adaptation of peripheral sense organs, and this is done operationally by demonstrating that after habituation, the effector system can be readily utilized for another response or the response can be elicited by a *qualitative* change in the stimulus used. Thus, habituation is a specific form of learning of immense adaptive usefulness in coping, physiologically, with a situation of unavoidable, repeated, or prolonged stimulation. This form of learning has been demonstrated in most aspects of autonomic regulation and has been reviewed at the behavioral, neuro-physiological (autonomic), and cellular levels.

An intriguing and poorly understood aspect of habituation is its

duration. Obviously, if habituation were permanent, adult organisms would be almost unresponsive except to stimuli never previously encountered. Some responses, particularly to weak stimuli, return within minutes or hours after the last stimulus presentation; others remain inhibited for days. If habituation is carried out over a number of days, the specific effect can last for weeks. Months later, after apparent recovery, some responses will rehabituate in one or two trials, indicating prolonged residual effect. Very painful and emotion-arousing stimuli or those related to the drives of hunger and sex show little or no long-term habituation.

There is evidence that habituation of autonomic responses involves central inhibitory systems and its rapidity is correlated with the rate of extinction of classically conditioned responses.

The second form of autonomic learning, the "conditional reflex" of Ivan P. Pavlov, has received more research attention than any other aspect of autonomic functioning. In this form of plasticity, the kinds of autonomic patterned responses described above (e.g., in exercise or digestion) come, at least partially, under the control of previously neutral signal stimuli because of repeated temporal association. The sign heralds the event and subsequently comes to elicit the response which could previously be elicited only by the event itself. The signal is generally termed the conditioned stimulus and the event, the unconditioned stimulus. This simple learning

paradigm has served as a useful model for the study of psychophysiological processes and even for the etiology of psychosomatic illness, wherein an organism responds in accordance with past experience in preference to current physical realities. To give a clinical example, classical conditioning may be involved when the asthmatic child in the city begins to wheeze at the sight of the car which usually takes him to the country, well before any rural allergens have reached his respiratory system.

Unfortunately, it has rarely been possible to study classical conditioning under the natural conditions of everyday life. The phenomenon remains a laboratory model and there are no data to tell us the extent to which this form of learning actually moulds specific autonomic responses in the individual throughout his development.

The range and variety of classical conditioning phenomena involving the ANS is truly impressive. Almost any stimulus which reaches the CNS, including visceral sensation ("interoceptive" stimuli) can acquire the capacity to activate almost any autonomic effector system, provided an unconditioned stimulus can be found which acts through the CNS to produce a response in the desired autonomic effector system. The signal (conditioned) stimulus must precede the physiological (unconditioned) by an interval ranging from less than half a second to as long as a minute for adequate conditioning to take place. Centrally acting drugs serve as well as physical stimuli, such as

electric shock, and with interoceptive stimuli much longer pairing intervals are effective. Generally, conditioned responses are small relative to the unconditioned responses, may fluctuate in amplitude after being established, and can even disappear after repeated elicitation. The timing of the conditioned response (whether "anticipatory" to the unconditional stimulus or coincident with it) and its magnitude are affected by: (1) the time interval between the signal and the physiological stimulus; (2) the intensity and nature of the physiological stimulus; the central state of the organism; and (4) the frequency, timing, and number of previous associative pairings. Repeated stimulation by a strong physiological stimulus may alter thresholds of response to mild signal stimuli, irrespective of associative pairing. This is often called "pseudoconditioning" and can be differentiated by the use of appropriate experimental controls.

This form of physiological learning can be conceptualized as a sophisticated extension of adaptive physiological organization. By this means the organism can prepare in advance for an environmental demand, such as a sudden burst of exertion, thus reducing the latency of appropriate physiological alterations, e.g., increased blood flow to the muscles. Indeed, some of the most elegant and complete descriptions of widespread classically conditioned cardiovascular responses come from the work of Rushmer and Smith on dogs repeatedly studied before treadmill-exercise tasks. Such studies approximate natural conditions in which the signal stimuli are

complex, often involving a whole environment including other people, and activate many sensory pathways. Likewise the unconditioned stimulus may also involve all aspects of ANS regulation in an organized pattern. These situations are very different from the excessively discrete stimuli used in the laboratory and a great deal less is known about the properties of classical conditioning under such circumstances. For instance, Hofer has shown that in people who are currently undergoing classical conditioning experience, naturally occurring life situations interact with the conditioned state to release the specific conditioned physiological response well in advance of its usual time of onset.

In the course of the exhaustive research conducted by Russian scientists on classical conditioning, a phenomenon began to emerge which has greatly extended the implications of learning for an understanding of ANS function in health and disease. For example, Lisina (cited by Razran) noted that although the usual classically conditioned vascular response to electrical shock was vasoconstriction, occasional vasodilatory responses took place. If the shock was made to terminate early whenever vasodilation occurred, there was little effect. However, if the subject was allowed to watch his own plethysmogram, he soon learned to vasodilate in response to the shock pairings and thus escape some of the electric shock. This suggested that the ANS response could be modified by an awareness of the consequences of the response, not simply by previous association of stimuli.

For many years it was believed that autonomically mediated behavior could be modified by classical but not by instrumental training methods. In the last few years new data have appeared to demonstrate that the ANS may also participate in the kind of learning which depends upon the consequences of a given response.

In an impressive series of experiments, Miller, DiCara, and others have demonstrated that salivation, heart rate, blood pressure, peripheral vasomotor activity, intestinal motility, renal and gastric blood flow can be either increased or decreased by a procedure of rewarding spontaneous fluctuations in the desired direction. The desired autonomic response can be progressively "shaped" to increasing magnitude by progressively altering the criterion level for reward by either brain stimulation or shock avoidance.

These experiments were carried out under curare with controlled positive pressure respiration as a control to rule out possible mediation of autonomic changes via reflex responses to a primary musculoskeletal maneuver, such as breath holding, carried out by the voluntary motor system. Initially conceived as a necessary control, it was found that the learning effect was much more readily obtained under curare than under natural conditions and this has raised problems of interpretation of their results. Does the explanation lie in the enormously simplified afferent feedback available to the curarized animal, resulting in a relative amplification of visceral information

necessary for instrumental learning? Or is it that curare and positive pressure respiration alter the central neural state so as to produce a unique functional organization not available to the animal under normal conditions? If the ANS *is* capable of instrumental learning during the natural state, why are the changes produced in both animals and man so small in magnitude and require so much training to achieve by present methods? These questions are currently under intensive investigation.

Answers to these problems bear directly on the implications this form of autonomic learning may have for the behavior of the ANS in health and disease. If environmental rewards occur following an autonomic response and if this "reinforcement" increases the likelihood and magnitude of the ANS response when the situation recurs, this may be the way in which specific autonomic responses, such as syncope or bronchoconstriction, become unusually frequent and severe in some people. This idea will be enlarged upon in the next section but it is clearly of considerable importance to understand the conditions controlling the ease and rapidity of instrumental learning in the ANS.

A major issue in our knowledge of how the ANS functions involves its specificity. In the same way that the ANS was thought to be capable only of classical conditioning, it was also, until recently, thought to be capable only of diffuse discharge. We have noted the tendency for patterns of integrated

activity involving all effector systems to be a common mode of operation. By differential reinforcement, again under curare, DiCara and Miller showed that it was possible for the ANS to dilate blood vessels in one ear and not in the other. Likewise, heart-rate increases could be produced without altering blood pressure and, vice versa, the same with heart rate and intestinal contraction. Clearly, discrete and specific alterations of ANS activity can be predictably demonstrated.

DiCara and Goesling and Brener present evidence that a *pattern* of musculoskeletal, respiratory, and cardiac activity is in fact conditioned under curare, although the first two are not evident until the animal recovers from the curare. Rats previously trained for high heart rates under curare are more active, more emotional by various criteria, and have much higher respiratory rates than those trained for low heart rates when the animals are replaced in the training situation without curare. What is actually learned is a pattern involving musculoskeletal, respiratory, and autonomic cardiac pathways. Further training without curare can separate the cardiac from the other physiological and behavioral changes, but no further increase in cardiac rate change is accomplished. Brener has shown in another way that musculoskeletal and cardiac changes are functionally interrelated and even centrally interdependent. Animals trained to be active to avoid electric shock, when subsequently trained to alter heart rate under curare, showed increased heart rate regardless of which direction of change they were being

trained for under curare. Those trained to inactivity before heart-rate training showed decreased heart rate, regardless of reinforcement contingencies under curare. Thus, the direction of heart-rate change under curare was more powerfully determined by their previous behavioral training than by the more immediate autonomic training under curare. These experiments suggest that there are important interactions between somatomotor and autonomic learning experience. An understanding of these interactions may take us a long way toward learning how these processes may determine autonomic responses to environmental events in natural life situations.

The role of this form of plasticity in the *internal* economy of the organism is also of considerable theoretical importance. For instance, to what extent are homeostatic regulatory processes acquired through learning rather than developed according to genetic plan? Miller et al. have shown that an excess of extracellular water or salt can function as a drive and that a return to normal water and electrolyte balance, accomplished by visceral hormonal and autonomic responses, can function as a reward in an experimental situation. The implication is that homeostatic autonomic responses may be acquired and shaped by the action of reward in the form of a return of the internal milieu to normal. Moreover, the imbalances caused by disease processes are countered by autonomic readjustments which may be learned in the same way through the effect of tending to return the internal state toward status quo. This important new hypothesis on the origin and

maintenance of homeostatic functioning in health and disease urgently needs experimental testing.

A parallel development accompanying the growth of interest in autonomic reward learning has been the attempt to apply these training techniques to the treatment of disturbed autonomic function, such as arrhythmias of neural origin and hypertension. These techniques will be reviewed in subsequent chapters on these disease states.

To return for a moment to the experiments described above the subjects did not change their autonomic response when rewarded by shock escape until they were provided with additional feedback over exteroceptive pathways by being allowed to watch the plethys-mograph write-out. Brener gave subjects an opportunity to hear their heart beat amplified and they were eventually trained to be able to press a button every time they felt their heart beat, in the absence of sound amplification. After this training in visceral awareness, the subjects were able to increase or decrease heart rate "voluntarily" to a significantly greater extent than control subjects.

By what strategies do subjects accomplish this "voluntary" control? Some use respiratory or musculoskeletal intermediary behavior, others attempt to create certain mental states, and still others cannot describe how it is done. Contrived strategies are not always the most effective. In applying

biofeedback to the therapeutic situation, no other reward is necessary to the patient than return of his biofeedback signal toward normal levels.

This work is in its infancy and requires a great deal more carefully controlled investigation, but it promises to open up new links between conscious experience and the autonomic nervous system.

Early Experience Effects

Mounting evidence over the past ten years has made it clear that behavior, visceral responses, and even survival of the adult under stress can be predictably influenced by alterations in early experience during development of the organism. Of the visceral alterations produced in this way, the pituitary adrenocortical system is the only one which has been extensively studied. There is enough direct evidence however, to conclude that autonomic responses can also be shaped by these long-term developmental interactions. If autonomic neural regulation and response patterning can be influenced by early experience, then knowledge about these processes may help us to understand how a particular adult can have acquired psychosomatic vulnerabilities.

In 1961, during John P. Scott's classic studies on socialization in dogs, his co-workers observed that if puppies were left in the company of other dogs without human contact for the first twelve weeks of life, they showed

heart-rate responses to electric shock at fourteen weeks of age which were significantly different from dogs which had had as little as one week "socialization" experience with people when they were seven-week-old puppies. If the week of socialization experience occurred either earlier or later than seven weeks it was less effective in altering both cardiac response and behavior. This age was thus described as a "critical" period for the effect of socialization in the dog. The influence of restricted as opposed to increased locomotor, sensory, and social experience on the development of heart-rate regulation has been further documented by two independent studies. They both showed higher heart rates in response to a variety of stimuli in adult rats which had been raised in early environments with increased stimulation. Restricted or isolated early living conditions, in contrast, predisposed to bradycardia in response to stimulation by noise. Handling of neonatal rat pups, known to produce an altered adrenocortical response to stress during adulthood, has been shown to increase the level of heart rate and decrease its variability during a period of stimulation of the adult rat by white noise. These demonstrations make the importance of early experience in the development of autonomic response tendencies clear but do not tell us *how* the experience comes to affect autonomic regulation in later life. As yet we cannot even say whether early handling works primarily by a direct stimulating effect on the pups or through altering maternal behavior toward those pups. Recent studies have shown that handling the mother can affect

adrenocortical reactivity of her offspring in later life and that separation of rat pups from their mother, at two weeks of age, produces a marked alteration in autonomic cardiac balance.

Studies have shown that the influence of early experience is not confined to small differences in autonomic response pattern but can reliably affect mortality rates from starvation, surgery, and metabolic derangement as well as modify susceptibility to experimental gastric-ulcer formation. In all these conditions, the ANS is known to play an important regulatory role and it is reasonable to suppose that altered ANS function may mediate these early experience effects.

Knowledge of the development of autonomic neural integration is just beginning to accumulate and our understanding of how early experience and its timing may shape the course of development is rudimentary. This is an area of active research interest which should contribute significantly in the next years to our understanding of the origin of psychosomatic illness.

Pathophysiological Mechanisms

Having outlined the functional characteristics of the ANS in relation to both the internal and the external environment, I will conclude and summarize by attempting to sketch how these characteristics may operate in the exacerbation or production of disease states during interaction of the

organism with its environment. I would like to emphasize how tenuous the links are between what we know of autonomic functioning and the production of illness in the organism. The natural history of man is characterized by repeated adaptive challenges posed by his social and physical environment. The predominant function of the ANS is not only to respond to the environment but to return to baseline, not only to react but to repair. As Richards has so elegantly described, medical illness can be characterized as disordered homeostatic balance. Yet little is known of the factors which sustain imbalance or cause prolonged over- and underresponse. New data suggest that homeostatic organization may be acquired through physiological learning, rather than be dictated by genetic mechanisms alone. If this is so, some individuals may acquire the potential for prolonged disorders of homeostatic balance and thus a proclivity toward illness. We do not yet have any clear idea of how or when such characteristics might be acquired.

The ANS, through its central neural integration, is one of the prime organizers of homeostasis, and we may justifiably examine its functional properties in search for the mechanisms of disordered function and look to the relationship of the organism with its environment as an important contributor to the etiology of illness. But in our present state of knowledge we must do so with the intent of generating testable ideas rather than outlining established principles.

Although homeostatic regulation is organized to return function within the ANS to a set level, priorities appear to exist so that homeostasis in one area of the system may be maintained at the expense of severe disequilibrium in another. The example was given of temperature homeostasis being maintained at the expense of water and electrolyte balance during heat stress, in order to illustrate the role of the ANS in determining the form of physiological disruption following environmental stress. Since there appear to be highly individual patterns of autonomic neural balance and integration among the effector systems, certain individuals may be more susceptible and others relatively resistant to disruption by an identical environmental stress. These individual patterns may be predominantly determined by genetic mechanisms or by previous environmental adaptations such as a high-salt diet. Furthermore, autonomic functions fluctuate in regular rhythms leading to a period during the twenty-four-hour cycle when susceptibility to under- or overresponse to a given stressor is relatively increased. During the course of development, autonomic balance changes markedly so that different life stages are associated with a greater likelihood of certain pathological responses. For example, clinicians are aware that autonomic responses to manipulation of the upper gastrointestinal (GI) tract, such as salivation, retching, and bradycardia are more intense during childhood and adolescence than in later life.

Autonomic responses to environmental stimulation and to mental and

physical tasks appear to have some immediate adaptive function in preparing the organism internally to function more effectively in its environment. However, the repeated, frequent elicitation of defensive, alerting, and exertional responses has been demonstrated to produce sustained hypertension, vascular and renal lesions, and increased mortality in animal colonies under specified conditions. Alterations of ANS function during altered states of consciousness, such as REM sleep, may precipitate episodes of congestive failure, arrhythmia or angina pectoris in cardiac patients because of the "flurries" of tachycardia, and bradycardia and vasoconstriction characteristic of the autonomic function during that state of sleep. Likewise, transient emotional states are associated with a wide variety of autonomic patterns and responses which may precipitate decompensation of chronic disease states. Stroebel95 has found evidence that certain emotional states cause a prolonged disruption of the organized patterns of circadian rhythmicity. The resulting autonomic disorganization may increase disease susceptibility. Avoidance learning contingencies may serve to perpetuate such disorders of central neural homeostatic control.

None of these interactions account for the clinically observed fact that some people are unusually prone to *highly specific* kinds of autonomic responses of extreme intensity, for example asthma, in the absence of allergenic stimulation. The facts on autonomic learning and early experience effects allow us to build a theoretical model for the acquisition of such highly

specific autonomic pathophysiologic response tendencies. It seems possible that a certain early experience occurring at a sensitive period may alter the genetically programmed development of reactivity in autonomic function, either through shifting baseline set point, variability, or the capacity to habituate. Such early experience may at the same time elicit a characteristic primitive emotional state. Then, through associative learning, a particular physiological response may become conditioned to signal stimuli which, at this development stage, characteristically precede physiological stimulation. The response is thus more frequently elicited and by ordinarily trivial stimuli. In addition, if the response tends to be followed by reward or by the avoidance of unpleasant events, instrumental conditioning may gradually strengthen and shape the autonomic response until a highly specific and intense physiological response is produced in that particular individual.

One may exemplify such a series of processes in the hypothetical development of bronchial asthma. A tendency toward respiratory hyperactivity may be set in motion by an early experience, such as maternal separation, which provokes repeated and prolonged crying, and a concomitant emotional state which may be termed “separation anxiety.” Subsequently, exposure to heavy concentrations of pollen precipitates asthma in association with environmental cues which thereafter acquire the capacity to elicit mild bronchoconstriction over autonomic pathways. The parents respond to the mild wheezing elicited by these conditioned cues with

exaggerated attention, gifts, and permission to avoid unpleasant duties. They may even cancel an intended departure from home. These rewards or "reinforcement," which may depend upon the emotional state generated by threatened separation, increase the likelihood and intensity of asthmatic episodes in the future. The child learns, perhaps without conscious awareness, that he can get what he wants by asthmatic breathing.

At this point, the emotional state elicited in this person by threatened separation has become associated (through classical and instrumental learning processes) with a highly specific autonomic response pattern: intense bronchospasm, mucous secretion, etc., that is, clinical asthma. Inborn autonomic correlates of an emotional state thus may become specifically modified by particular developmental experiences. The emotional state, however, is subject to further modification by a number of other psychological processes and experiences which may even disassemble this organization and "cure the disease."

The emotional states deriving from the early separation experience, and the human relationships built upon them, thus may become interwoven with the specific physiological effects of the experience on the development of the child's respiratory system. Both associative and instrumental learning may function to stamp in and intensify what might otherwise be a mild and transient period of childhood wheezing. Further learning and emotionally

trying human relationships may finally generate the severe reactive asthma which has earned the term "psychosomatic."

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