24
Autonomic Nervous System Testing

Frederick K. Nahm and Roy Freeman

Summary

Autonomic testing encompasses an array of procedures that can be used to assess a variety of symptoms ranging from lightheadedness and dizziness to anhydrosis to constipation and urinary incontinence. A number of procedures are available for testing of the many varied aspects of both the parasympathetic and sympathetic nervous systems. These tests include Valsalva maneuver testing, RR interval testing, tilt-table testing, microneurography, and the thermoregulatory sweat test. This chapter reviews the basic neuroanatomy and neurophysiology of the autonomic nervous system and the tests that are most effective in their evaluation.

Key Words: Anhydrosis; hypotension; lightheadedness; neuropathy; parasympathetic; sympathetic.

1. INTRODUCTION

Disorders of the autonomic nervous system (ANS) can be found in many conditions that span the disciplinary boundaries of medicine. The neurophysiological evaluation of the human autonomic nervous system function is challenging because most autonomic structures are located at a distance from the skin, and, thus, less amenable to direct observation or study. In addition, most neurophysiological measures of the ANS reflect end-organ function (smooth muscle, cardiac muscle, and glandular organs), rather than direct neural activity in the sympathetic and parasympathetic nerves. Despite these methodological difficulties, there are a number of clinically useful techniques that test the functional integrity of the sympathetic and parasympathetic nervous system. The aim of this chapter is to provide a basic understanding of neurophysiological testing methods that are used to evaluate autonomic disorders.

Neurophysiological tests of autonomic function are extensions of the clinical exam, and their appropriate use requires a thorough history and physical examination. In addition, a careful review of autonomic symptoms should be taken, with attention to systems commonly affected by autonomic dysfunction. As in all clinical tests, the pretest clinical probability affects the power of ANS testing, and a clear, well-formulated question should precede ANS testing. A brief list of the more common autonomic symptoms are listed in Table 1. A few of the more common indications for ANS testing are listed in Table 2.

2. NEUROANATOMIC AND NEUROPHYSIOLOGICAL PRINCIPLES

A systematic approach to ANS testing is important given its neuroanatomical complexity. A useful conceptual approach for understanding sympathetic and parasympathetic function is to think in terms of neuronal circuits and autonomic reflex arcs (Fig. 1). Afferent information arises

From: *The Clinical Neurophysiology Primer*
Edited by: A. S. Blum and S. B. Rutkove © Humana Press Inc., Totowa, NJ

Table 1
Common Autonomic Symptoms

Orthostatic intolerance
Dizziness
Lightheadedness
Fatigue
"Coathanger" headache
Nausea
Palpitations
Near-syncope and syncope
Genitourinary
Bladder urgency or frequency
Incontinence
Nocturia
Erectile dysfunction
Ejaculatory disturbances
Gastrointestinal
Diarrhea
Constipation
Fecal incontinence
Postprandial fullness, cramping, or bloating
Sudomotor
Hyperhidrosis
Hypohidrosis and anhidrosis

Table 2
Indications for Autonomic Nervous System Testing

Syncope
Central autonomic degenerations (e.g., multiple system atrophy with autonomic failure, and Parkinson disease)
Pure autonomic failure
Postural tachycardia syndrome
Autonomic and small-fiber peripheral neuropathies (e.g., diabetic peripheral neuropathy, amyloid peripheral neuropathy, and hereditary peripheral neuropathies)
Sympathetically mediated pain
Evaluating response to therapy
Differentiating benign symptoms (e.g., dizziness) from life-threatening autonomic disorders

from end-organ receptors, such as baroreceptors in vessel walls, and mechanoreceptors and metaboreceptors in skeletal muscle. Signals arising from these structures are directed to central autonomic structures via unmyelinated and myelinated autonomic nerves. The nucleus tractus solitarius, located in the dorsal medulla, receives much of the afferent peripheral autonomic input. This structure has reciprocal connections to central regions regulating both sympathetic and parasympathetic function and plays an important role in feedback regulatory circuits.

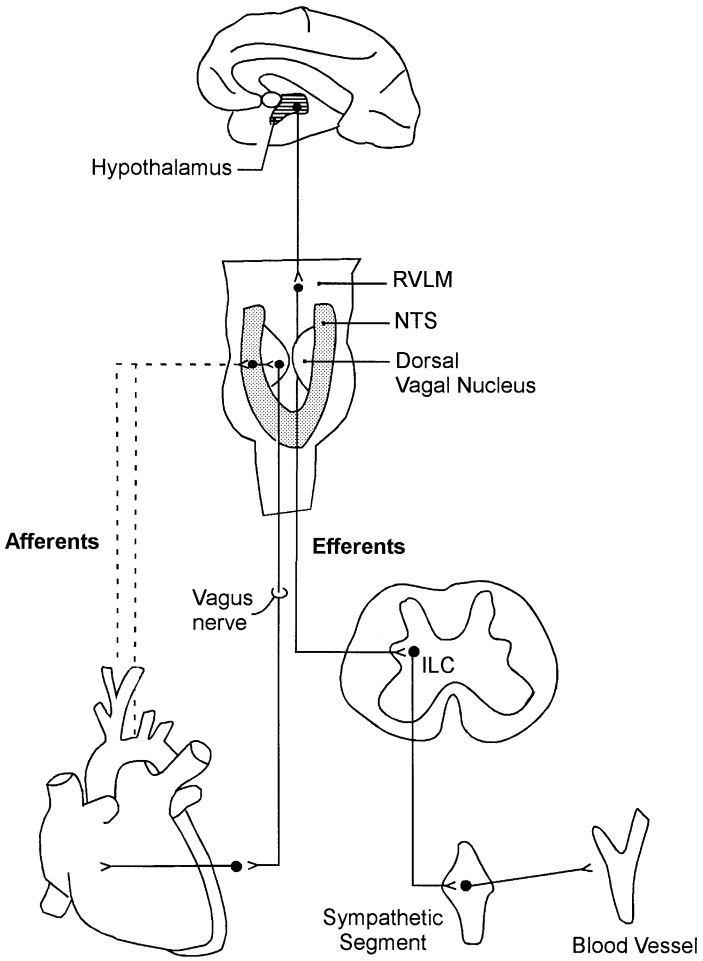

Fig. 1. Schematic representation of autonomic reflex arc, showing baroreceptor afferents in dashed lines, central processors, and efferents (solid lines) to end organs. ILC, intermedial lateral columns; RVLM, rostral ventral lateral medulla; NTS, nucleus tractus solitarius.

Central regions with input to sympathetic preganglionic neurons centers include the paraventricular nuclei of the hypothalamus, the amygdala, and the insular and medial prefrontal cortices. Preganglionic sympathetic neurons are also located in the rostral ventrolateral medulla, the caudal ventrolateral medulla, the caudal raphe nuclei, and the A5 region of the pons.

Efferent parasympathetic fibers originate in the Edinger–Westphal nucleus, ciliary ganglion, superior and inferior salivary nuclei, otic ganglion, and the nucleus ambiguous and the dorsal motor nucleus of the vagus. These fibers are carried in cranial nerves III, VII, IX, and X, and synapse on both end organs and parasympathetic ganglia located within or in close proximity to their target organs. Preganglionic parasympathetic fibers related to genitourinary function originate in the spinal cord at sacral cord levels 2, 3, and 4. Efferent preganglionic sympathetic fibers originate in the intermediolateral cell columns at levels T1–L2. These fibers synapse on postganglionic fibers in paravertebral, prevertebral, and previsceral ganglia.

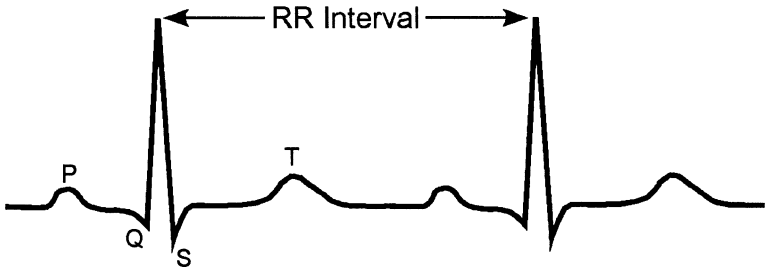

Fig. 2. The RR interval is the duration, measured in milliseconds, between successive R waves in the QRS complex.

3. PATIENT PREPARATION FOR AUTONOMIC TESTING

Before ANS testing, patients should refrain from heavy meals, coffee, and nicotine for at least 3 to 4 h before studies. Medications with either anticholinergic effects or those with α- and β-receptor agonist or antagonist activity should be withheld (if medically appropriate) 24 to 48 h before testing, because these can significantly affect the outcome of ANS tests.

Most autonomic testing sessions are 60 to 90 min. Patients should wear loose-fitting clothes for comfort and to facilitate the application of cardiac electrodes and blood pressure (BP) cuffs.

4. ELECTROPHYSIOLOGICAL METHODS

4.1. Heart Rate Recording and the RR Interval

Heart rate (HR) is routinely recorded with a three-lead electrocardiograph (ECG) machine. Tests evaluating HR variability can only be performed in the setting of sinus rhythm. The ECG leads are placed at anterior chest locations, which minimize movement artifact, and the reference electrode is usually placed at the mid-axillary line at approximately the T4 level. Autonomic tests of HR variability may be based on HR measure in beats per minute or its inverse, the RR interval, measured in milliseconds (Fig. 2).

4.2. BP Recording

BP during autonomic testing can be measured intermittently or continuously. Some methods rely on brachial artery cuffs, whereas others use devices that are applied to the wrist or the finger. The intermittent recording techniques rely on occlusive cuff methods. Techniques for detecting arterial lumen opening include auscultatory and oscillometric methods. Auscultation for Korotkoff sounds is a widely available, and invaluable, bedside tool. The oscillometric technique is based on the observation that during cuff deflation, the point of maximal oscillation between systolic and diastolic pressure corresponds to the mean arterial pressure. Although both the auscultatory and oscillometric techniques are relatively easy to perform, they provide only periodic sampling of BP.

Plethysmography and arterial tonometry are methods used for continuous, beat-to-beat, noninvasive BP recording. Plethysmography is an indirect measure of BP, whereby the pulse pressure is derived from the blood volume. The volume clamp method of Peñaz, also called arterial counterpulsation, uses a servo-loop circuit that continuously counterbalances arterial pressure, thereby clamping the volume of blood flow to maintain a transmural pressure of

zero. The counterpulsation pressure provides a real-time measure of arterial pulse pressure. The volume clamp technique of Peñaz has been used with digital pressure cuffs and finger photoplethysmography. A potential drawback to this method is its sensitivity to decreases in distal limb temperature, which may significantly alter the measured BP.

Arterial tonometry is a method in which arrays of pressure sensors compress and partially flatten (applanation) an artery at a constant pressure. The intra-arterial forces measured by the sensor array are then translated into arterial pressure waveforms displayed in real time. The tonometric sensors, which are placed over the radial artery, may be affected by both improper sensor placement as well as tremors. Both methods may be inaccurate in subjects with peripheral vascular occlusive disease, and both are dependent on arm position. Recordings should be made with the arm abducted or elbow flexed so that the recording site is at the level of the heart throughout autonomic testing.

During formal tests of autonomic function, both intermittent and continuous BP recordings are usually obtained. Oscillometric BP recordings may be used to verify the accuracy of the continuous BP recordings, and may serve as a more reliable means of BP recording in the event of marked decreases in BP.

5. PARASYMPATHETIC FUNCTION TESTS

Neurophysiological tests of cardiovascular parasympathetic function evaluate the integrity of a reflex arc that includes the vagus and glossopharyngeal nerves; cardiopulmonary baroreceptors located in structures, such as the carotid sinus and aortic arch; pulmonary receptors; cardiac atria and ventricles; and pulmonary arteries and veins. Afferent signals from the receptors are carried in both myelinated and unmyelinated fibers, and travel in sympathetic nerves to the spinal cord and in the vagus and glossopharyngeal nerves to the nucleus tractus solitarius and other areas in the medulla that play a role in BP and HR control.

5.1. HR Response to Valsalva Maneuver

The Valsalva ratio (VR) is an index of HR changes that occur during a Valsalva maneuver (*see* Table 3). The Valsalva maneuver is performed by having the patient exhale for 15 s, while maintaining an expiratory pressure of 40 mmHg. Expiratory pressure can be measured by having the patient blow into a mouthpiece connected to a pressure transducer. Forced expiration to maintain an expiratory pressure of 40 mmHg produces the most consistent change in BP. Typically, a baseline HR and BP will be obtained during 3 min before the Valsalva maneuver. The patient is then instructed to inhale deeply, exhale completely, then take another deep breath in and blow into the mouth piece. Both HR and BP are recorded during the maneuver and up to 60 s after the Valsalva maneuver is terminated. A mild degree of lightheadedness is often reported during this procedure. Because of the need for prolonged expiratory effort, the elderly and those with any underlying pulmonary disorders may find the Valsalva maneuver difficult to perform. Typically, one to two trials are obtained for analysis, with an adequate time between trials (3–5 min) to allow subjects to return to a baseline state. Because intraocular pressure increases during Valsalva maneuver, recent retinal surgery or hemorrhage is a relative contraindication to performing this test.

The VR is a measure of the HR response to BP changes resulting from the mechanical and cardiovascular effects of the Valsalva maneuver. There are four phases of BP, designated I to IV, which delineate the cardiovascular changes during the Valsalva maneuver. Phase I consists of a transient rise in BP that results from the increased intrathoracic and intra-abdominal

Table 3
Valsalva Ratio

Stimulus	Expiration of 40 mmHg for 15 s
Afferent	Baroreceptors, glossopharyngeal, and vagus nerves
Central	Nucleus tractus solitarius
Efferent	Vagus and sympathetic nervous system
Response	1. Heart rate response to blood pressure changes 2. Fall and rise in blood pressure (phases I–IV)

pressures. During phase II, there is a fall and recovery of BP. During phase III, there is a decrease in BP caused by the release of intrathoracic pressure. During phase IV, there is an "overshoot" caused by the increase cardiac output into a vasoconstricted peripheral circulation.

As the BP falls in phase II, there is an increase in HR caused by parasympathetic withdrawal that is then followed by sympathetic activation. This results in an increase in HR during and shortly after the Valsalva maneuver. In response to the BP overshoot during phase IV, approx 15 to 30 s after the end of the maneuver, the HR falls and produces a transient bradycardia that persists, in the normal state, until after the BP overshoot. This results in the minimum HR. The VR is calculated as the maximum HR, which occurs during or shortly after the Valsalva maneuver, divided by the minimum HR, which occurs after the cessation of the Valsalva maneuver (VR = max HR/min HR). A normal HR and BP response to Valsalva maneuver is depicted in Fig. 3.

A normal VR reflects an intact baroreceptor-mediated rise and fall in HR. The VR values are age related, and decline with increasing age. A reduced VR reflects baroreceptor and cardiovagal dysfunction. However, it is important that an adequate and steady expiratory pressure is maintained during the maneuver for these results to be meaningful.

5.2. HR Variability With Respiration (Respiratory Sinus Arrhythmia)

The expiratory/inspiratory (E/I) ratio, similar to the VR, is a measure of parasympathetic function (*see* Table 4). Timed breathing potentiates the normal sinus arrhythmia that occurs normally during respiratory cycles. The physiological mechanism of respiratory sinus arrhythmia is complex and includes pulmonary stretch and cardiac mechanoreceptor activation, baroreceptor activation, local cardiac reflexes and central factors. During inspiration, there is a reflex withdrawal of parasympathetic activity, increased excitability of cardiac pacemaker cells in the sinoatrial node, and an increase in HR. Respiratory sinus arrhythmia provides a measure of parasympathetic control of HR variation throughout the respiratory cycle.

The respiratory sinus arrhythmia is recorded with the patient supine and breathing at a fixed rate. A respiratory frequency of six breaths per minute, with slow inhalation and exhalation (5 s each) provides close to maximum HR variability (Fig. 4). The timed breathing is performed with the aid of either verbal coaching, or an electronic visual cue. This is a safe, easily performed test, without contraindications. Typically, six to eight cycles are recorded, and one to two trials are performed. The variation in HR across this cycle of six to eight breaths is often expressed as the mean difference between the maximum and minimum HR. Alternatively, one can calculate the E/I ratio, which is the sum of the longest RR intervals divided by sum of the shortest RR intervals (E/I = Σ longest RR/Σ shortest RR). Other

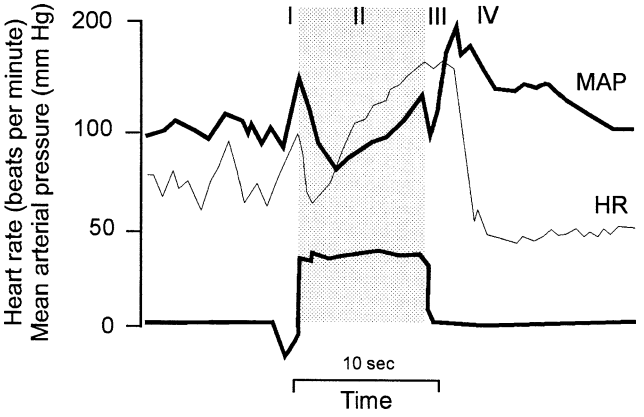

Fig. 3. Blood pressure and heart rate response to Valsalva maneuver. Top tracing represents mean arterial pressure (MAP) with phases denoted by Roman numerals. Middle tracing represents heart rate (HR). Bottom tracing shows expiratory pressure during Valsalva maneuver. The shaded area delimits both early and late phase II.

Table 4
Expiratory/Inspiratory Ratio

Stimulus	Deep breathing (6 cycles/second)
Afferent	Pulmonary receptors, cardiac mechanoreceptors, vagus and glossopharyngeal nerves, respiratory center
Central	Nucleus tractus solitarius
Efferent	Vagus
Response	1. Heart rate increase during inspiration 2. Heart rate decrease during expiration

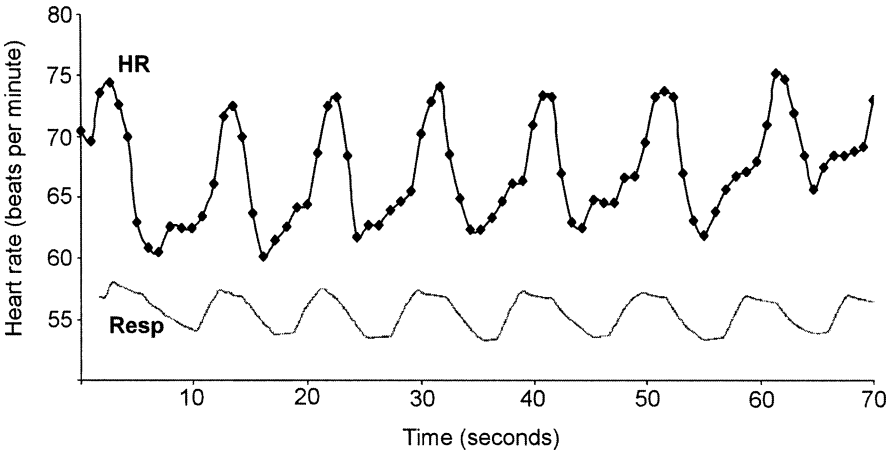

Fig. 4. Top tracing shows the variation in heart rate (HR) during metronomic breathing. Lower trace represents corresponding respiratory (resp) pattern.

analyses used to describe HR variability include measurements of HR standard deviation, mean consecutive difference, mean square consecutive difference, mean circular resultant, and power spectral analysis.

Table 5
Active Standing (30:15 Ratio)

Stimulus	Decreased central blood volume
Afferent	Baroreceptors, ergoreceptors, "central command," and vagus and glossopharyngeal nerves
Central	Nucleus tractus solitarius, rostral ventrolateral medulla
Efferent	Vagus
Response	1. Heart rate increase at beat ~15 2. Heart rate decrease at beat ~30

HR variability with respiration decreases with increasing age. Reduced HR variability with respiration can be observed in cases of autonomic failure caused by autonomic peripheral neuropathies and central autonomic degenerations. Other factors known to influence the HR response to deep breathing include poor respiratory effort, hypocapnia, salicylates, positioning, and obesity.

5.3. The 30:15 Ratio

The 30:15 ratio, similar to the VR and E/I ratio, is a measure of parasympathetic cardiovagal function (*see* Table 5). Immediately after standing, there is an increase in HR that reflects an exercise reflex and withdrawal of parasympathetic tone. There is a further HR increase at approx 15 s that reflects a compensatory response to decreased venous return and decreased cardiac output and a fall in BP. This is followed by a second period of relative bradycardia at approx 30 s. The 30:15 ratio is the RR interval at approx 30 s, divided by the RR interval at approx 15 s.

A baseline HR should be obtained in the supine position, and the patients are then asked to quickly stand upright onto their feet. A chair may be placed behind subjects to sit on should they become symptomatic suddenly. The HR variability is recorded for at least 1 min of active standing. A normal ratio is greater than unity, and reflects intact vagally mediated HR variation. An abnormal ratio suggests parasympathetic cardiovagal dysfunction. A number of general medical conditions, such as hypovolemia, medical deconditioning, and hypothyroidism can lead to misinterpretation of the 30:15 ratio and, thus, these factors should be taken into account when interpreting the test results.

6. SYMPATHETIC FUNCTION TESTS

6.1. Head-Up Tilt-Table Testing

During the tilt-table test, the BP and HR response to an orthostatic challenge is used to provide a measure of sympathetic function (*see* Table 6). Similar to the early response to active standing, the early cardiovascular response to head-up tilt is largely caused by blood volume redistribution to the lower extremities. However, tilt-table testing is more sensitive to such redistribution because there is minimal contraction of lower extremity muscles, thus, further reducing the amount of venous return. This test is used to assess orthostatic intolerance caused by sympathetic nervous system dysfunction and also to uncover a predisposition to neurally mediated (vasovagal syncope).

The patient lies supine on the tilt table. Beat-to-beat and oscillometric BP instruments are attached to each arm. EKG monitoring should take place throughout the test. A large waist

Table 6
Tilt-Table Testing

Stimulus	Decreased central blood volume
Afferent	Baroreceptors, vagus and glossopharyngeal nerves
Central	Nucleus tractus solitarius, rostral ventrolateral medulla, hypothalamus
Efferent	Sympathetic vasomotor
Response	1. Pattern, rate, and degree of blood pressure changes 2. Heart rate rise or fall

belt should be placed around patients to secure them in case of syncope or unexpected falls. Other safety measures include the availability of cardiovascular medications, including atropine, and a resuscitation cart that can be used in the event of cardiac asystole and other unexpected cardiac arrhythmias.

Once the patient is comfortable, with feet resting on the footboard, a baseline BP is recorded for at least 3 min. The patient is then slowly tilted upright to an angle of 60° to 80°. During testing, the patient is asked to report any symptoms. Both BP and HR are recorded throughout tilt-table testing, after which the patient is returned to a horizontal supine position. BP and HR should be monitored in the supine position until patients return to baseline. Tilt-table test results are influenced by a number of conditions, such as hypovolemia, cardiovascular deconditioning, medications, hypothyroidism, infection and sepsis, and reduced myocardial function. These conditions must be accounted for during the interpretation of abnormal tilt-table findings.

Some laboratories use pharmacological measures to potentiate the orthostatic challenge of head-up tilt. Intravenous administration of isoproterenol, a β-adrenergic agonist that increases ventricular contractility and HR, is frequently used. This intervention may increase the sensitivity of the test but is associated with reduced specificity. In addition, the sight of needles and blood, as well as pain may further reduce the specificity of the test. The use of sublingual nitroglycerin may increase the sensitivity of the test while avoiding these precipitants.

A normal tilt-table test is one in which there are no symptoms, and only a modest fall in systolic BP. Orthostatic hypotension is defined as a decrease in systolic BP of greater than 20 mmHg, diastolic BP greater than 10 mmHg accompanied by symptoms of orthostatic intolerance. The pattern, the temporal characteristics, and the degree of changes that occur in both the BP and HR define the test abnormality. The use of the term "positive tilt-table test" is incomplete, uninformative, and should be avoided.

Three well-described patterns of neurally mediated syncope can occur during head-up tilt-table testing:

1. Vasodepression resulting in hypotension without bradycardia.
2. Cardioinhibition with a marked bradycardia (fewer than 40 beats per minute) with or without significant hypotension.
3. Mixed, with both bradycardia and hypotension (Fig. 5).

6.2. Valsalva Maneuver

As discussed in Subheading 5.1., there are four described phases of the Valsalva maneuver. Phase I is an initial rise in BP, largely caused by mechanical factors. Phase II is divided into early (II_e) and late (II_l) components. The fall in BP during phase II_e is caused by a decrease in preload and cardiac output. Phase II_l represents a rectification of the fall in BP

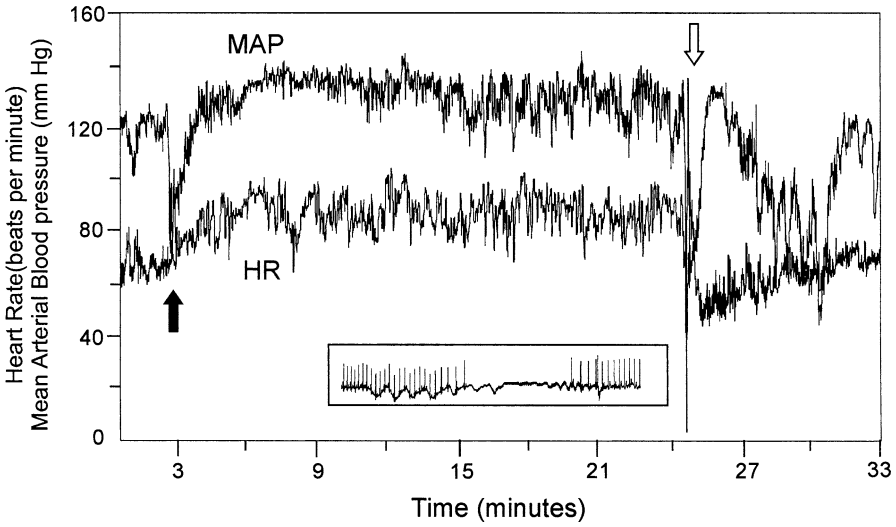

Fig. 5. Blood pressure and heart rate (HR) response to prolonged 45-min tilt-table test at 60° of upright position. Top tracing is mean arterial blood pressure (MAP) curve; bottom tracing is HR. The dark arrow depicts the point of head-up tilt. The hollow arrow depicts return to supine position. At 25 min into the test, there is a precipitous fall in both mean arterial pressure and heart rate. The inset is a sample of the ECG occurring at the 25 min mark, which shows heart rate slowing and asystole. *See* text for further details.

caused by an α-adrenergic sympathetically mediated increase in total peripheral vascular resistance and the increase in HR. The abrupt fall in BP during phase III represents a withdrawal of intrathoracic pressure at the termination of forced expiration. Phase IV, the last phase of the Valsalva maneuver, reflects a BP overshoot caused by the increase in α-adrenergic-mediated peripheral vascular resistance, and β-adrenoreceptor-mediated increase in cardiac output.

An abnormal response to the maneuver includes an excessive BP fall in the early phase II, an absent or incomplete recovery failure in late phase II, and/or the absence of a BP overshoot during phase IV. These abnormalities are observed in the presence of sympathetic dysfunction.

6.3. Sympathetic Cholinergic Sweat Function

The best-known neurophysiological test of sympathetic sudomotor function is the sympathetic skin response (SSR), or galvanic skin response. Increased sympathetic nerve fiber sudomotor activity causes release of sweat from glands in the skin, which can be detected as a change in surface conductivity. A standard EMG instrument can be used to measure this response. A small recording electrode is attached to the palmar and dorsal surface of both hands and feet, with a long sweep speed (10 s) setting, and a bandpass filter of 1 Hz to 2000 Hz. After a stable baseline is obtained, a stimulus is administered and the SSR is recorded. Any stimulus that activates the sympathetic system can be administered, such as an electrical stimulus, a loud noise, or a bright light. Simultaneous recording from both hand and foot can be performed, which demonstrates the length-dependent latency difference between these sites. Typically, three to four trials are obtained at each site. A normal SSR is a monophasic or biphasic deflection that habituates with time and repeated trials (Fig. 6). An abnormal

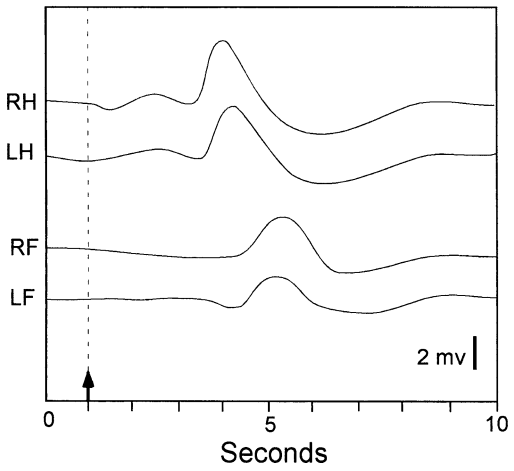

Fig. 6. Sympathetic skin response (SSR) measured from the left hand (LH) and right hand (RH), and left foot (LF) and right foot (RF) after a 30-mA stimulation to the proximal left upper extremity. The onset of the stimulus is denoted by the arrow and the dashed line. Note the delay in onset in the SSR recorded from the feet as compared with the arms.

response is an absent SSR, and reflects sympathetic sudomotor dysfunction. This test does not differentiate between preganglionic or postganglionic sympathetic dysfunction.

In the silastic imprint test, a plastic or silicone film is applied to the area of sweat gland activity provoked by the iontophoresis of a cholinergic agonist. The film is then removed, and the number of active sweat glands, their density, and the volume of sweat secreted can be determined by digital image analysis.

The thermoregulatory sweat test is performed by the application of an indicator, such as alizarin red, which changes color in the presence of moisture. The indicator is applied to the body of the patient, who is then placed in a thermally controlled environment, and the core temperature is raised above baseline. The pattern of color changes, which can be expressed as percentage of body surface, is used to quantify hypohypohidrosis and anhidrosis.

Iontophoresis of cholinergic agonists can also be used to evoke an axon reflex-mediated response from a more distal population of sweat glands. The response is recorded using a sudorometer, which measures changes in humidity resulting from sweat production. This quantitative sudomotor axon reflex test (Q-SART) can be used to measure both sweat volume and sweat pattern (Fig. 7). It is largely a measure of postganglionic sympathetic function, but may be reduced with severe preganglionic disorders.

7. MICRONEUROGRAPHY

Intraneural microneurography enables the direct measurement of muscle sympathetic nerve activity. A tungsten microelectrode of approx 5 μm in size is inserted into a fascicle of a distal sympathetic nerve to the skin or muscles. Using this technique, sympathetic outflow to skin and muscle can be measured at rest and in response to various physiological perturbations (Fig. 8). Muscle sympathetic nerve activity, consisting predominantly of efferent muscle blood vessel vasoconstrictor impulses, are grouped in relationship to the cardiac rhythm. Skin sympathetic activity consists of vasoconstrictor impulses to skin capillaries, arteriovenous shunts, and sudomotor and pilomotor impulses. They appear as irregular bursts

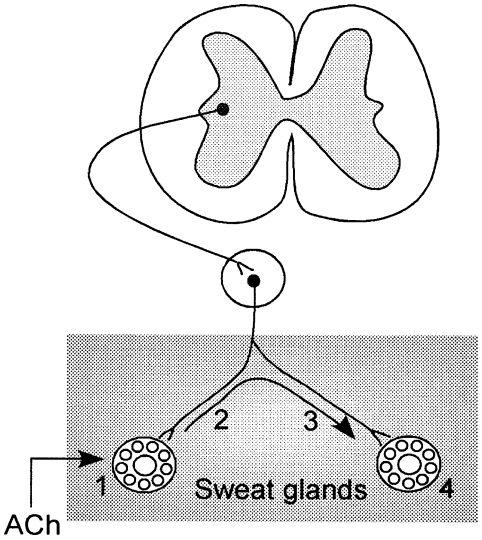

Fig. 7. Neurophysiology of the axon reflex test. Acetylcholine (ACh) is iontophoresed onto a sweat gland **(1)**, initiating an antidromic signal **(2)** in the distal postganglionic sympathetic fiber, which is then transmitted orthodromically **(3)** down an axon branch, stimulating glandular secretion at a distal site **(4)**. The hatched area represents structures within the skin.

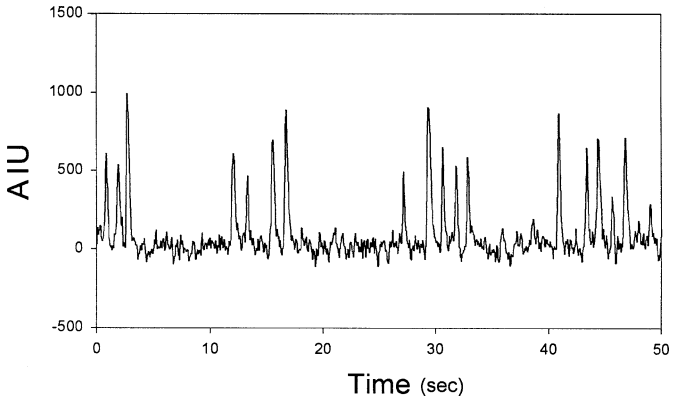

Fig. 8. Muscle sympathetic nerve activity displayed as integrated units (AIU) in response to sympathetic activation provoked by a nitroprusside bolus.

of varying duration, often occurring in relationship to the respiratory rhythm. This technique is primarily used in research, rather than in clinical laboratories.

SUGGESTED READING

Clinical autonomic testing report of the therapeutics and technology assessment subcommittee of the American Academy of Neurology. Neurology 1996;46:873–880.

Low PA. Laboratory evaluation of autonomic function. In: Clinical Autonomic Disorders, 2nd ed. (Low PA, ed.). Lippincott-Raven, Philadelphia, PA, 1997.

Primer on the Autonomic Nervous System (Robertson D, Low PA, Polinsky RJ, eds.). Academic Press, San Diego, CA, 1996.

Autonomic Failure—A Textbook of Clinical Disorders of the Autonomic Nervous System, 4th ed. (Mathias CJ, Bannister R, eds.). Oxford University Press, Oxford, England and New York, NY, 2001, p. 592.

Freeman R. Noninvasive evaluation of heart rate variability. In: Clinical Autonomic Disorders, 2nd ed. (Low PA, ed.). Lippincott-Raven, Philadelphia, PA, 1997, pp. 297–307.

The Autonomic Nervous System: An Introduction to Basic and Clinical Concepts, 5th ed. (Appenzeller O, Oribe E, eds.). Elsevier Science, New York, NY, 1997, p. 868.

REVIEW QUESTIONS

1. HR variability with respiration is a measure of:
   A. Parasympathetic nervous system function.
   B. Sinus arrhythmia.
   C. Vagal nerve activity.
   D. All of the above.
2. Head-up tilt-table testing may be used to measure:
   A. Parasympathetic nervous system function.
   B. Sympathetic nervous system function.
   C. A predisposition to vasovagal syncope.
   D. B and C.
3. A normal early phase II in the Valsalva maneuver refers to:
   A. HR increase.
   B. HR fall.
   C. BP overshoot.
   D. BP fall.
4. A decrease in the RR interval occurs when:
   A. The HR increases.
   B. The HR decreases.
   C. Vagal nerve activity increases.
   D. Vagal nerve activity decreases.
   E. E and D.
   F. B and C.
5. Which of the following agents can be used to induce axon reflex sweating:
   A. Isoproterenol.
   B. Propranolol.
   C. Nitroprusside.
   D. Acetylcholine.
6. The E/I ratio reflects:
   A. Sympathetic nervous system function.
   B. Parasympathetic function.
   C. BP fluctuations.
   D. HR variability.
   E. A and C.
   F. B and D.
7. The Valsalva maneuver is primarily used to evaluate:
   A. Sympathetic autonomic function.
   B. Parasympathetic baroreceptor function.
   C. A subject's expiratory capacity.
   D. A and B.
   E. A, B, and C.
8. The patterns of neurally mediate syncope include:
   A. Vasodepression.
   B. Mixed.

C. Cardioinhibitory.
D. All of the above.

9. Intravenous isoproterenol administered during a tilt-table test may:
   A. Increase HR.
   B. Reduce the specificity of the test.
   C. Increase cardiac contractility.
   D. All of the above.
10. The sudomotor axon reflex test is primarily a measure of these fibers:
   A. Preganglionic sympathetic cholinergic.
   B. Preganglionic sympathetic adrenergic.
   C. Postganglionic sympathetic cholinergic.
   D. Postganglionic sympathetic adrenergic.

REVIEW ANSWERS

1. The correct answer is D. The RR interval is the time between successive QRS complexes, and is a measure of cardiac vagal outflow. During normal breathing, a sinus arrhythmia can be observed in the RR interval, which is a normal physiological condition.
2. The correct answer is D. The head-up tilt-table test is used to assess orthostatic tolerance in patients with orthostatic hypotension caused by sympathetic nervous system dysfunction. It is also used to demonstrate a predisposition to neurally mediated syncope.
3. The correct answer is D. The early phase II section of Valsalva maneuver refers to the fall in BP that occurs during forced expiration. A BP overshoot can also be observed during phase IV of the maneuver; this overshoot occurs after the termination of forced expiration.
4. The correct answer is E. The RR interval is a measure of the time (in milliseconds) between successive QRS wave complexes. A decrease in the RR interval occurs when the HR increases. Because HR is under vagal control, a decrease in the RR interval, corresponding to an increase in the HR, occurs with the withdrawal of parasympathetic tone observed during a decrease in vagal nerve activity.
5. The correct answer is D. The cholinergic agonists are used to provoke axon reflex-mediated sweating. These agents are used to measure sudomotor function in the quantitative sudomotor axon reflex test and the silastic imprint method.
6. The correct answer is F. The E/I ratio is a measure of sinus arrhythmia. It is largely an index of cardiac vagal parasympathetic activity.
7. The correct answer is D. The HR and BP response to Valsalva maneuver is influenced by both the sympathetic and parasympathetic nervous system. Although an adequate forced expiration of 40 mmHg for 10 to 15 s is required to obtain reliable data during the Valsalva maneuver, it is not a formal test of pulmonary capacity or forced expiratory volume.
8. The correct answer is D. There are three patterns of cardiovascular responses that have been described during neurally mediated syncope. Vasodepression refers to a primary fall in BP without significant HR changes. The mixed form observed during head-up tilt-table testing is characterized by both hypotension and relative bradycardia, and cardioinhibitory neurally mediated syncope refers to a primary bradycardia below 40 beats per minute.
9. The correct answer is D. Intravenous isoproterenol increases cardiac inotropy and chronotropy. Although this intervention increases the sensitivity of the test, it reduces the specificity and can result in false positive studies.
10. The correct answer is C. The sudomotor axon reflex test is based on the fact that postganglionic nerve fibers can be antidromically stimulated by the application of a cholinergic agonist to the skin. This results in a signal traveling to a branch point, and then orthodromically down an adjoining postganglionic fiber, which results in the release of acetylcholine and the stimulation of eccrine glands in the skin. This test is used to evaluate the postganglionic sympathetic cholinergic system.