Abstract
Recent advances in computer technology have made it possible to noninvasively determine fast and dynamic changes in autonomic nervous activity in humans. Power spectral analysis of heart rate variation, beat-to-beat blood pressure analysis, skin blood flow by the laser Doppler technique, sensitive sudorometry and direct measurement of sympathetic nervous discharge have been successfully applied in adults, but there are still only few studies reported in children and adolescents. This article reviews the usefulness of these autonomic function tests in the pediatric field including reliability and methodological limits. Power spectral analysis of heart rate variability seems to be a new potential method, but there have been only few studies in children. Orthostatic maneuvers with noninvasive beat-to-beat measurement of finger arterial pressure, especially during active standing, is useful for the evaluation of orthostatic intolerance in children as well as adults with autonomic failure. A new pharmacological method using multiple autonomic agents might indicate a more precise information including alpha- and beta-adrenoceptor sensitivity. It should be realized that a single test cannot identify impaired autonomic functions, and a combination of several autonomic tests should be employed. Moreover, age-related changes and racial differences in autonomic function should be considered when interpreting obtained results.
Introduction

“Autonomic Function Tests in Children in the Past”

Since autonomic function tests are not commonly used in daily pediatric practice, methodology and usefulness of these tests have not been previously assessed satisfactorily in children. Most pediatricians might be puzzled as to what tests should be performed for evaluation in patients who are suspected of autonomic disorders.

In conventional autonomic function tests the pattern of blood pressure and heart rate responses to physical stimuli were used including deep breathing, Valsalva’s maneuver, postural change and hand grip [1], on the basis that cardiovascular responses reflect sympathetic and vagal activity and the interaction between both neural systems. These tests are simple and are easily done in daily clinical practice. However, the obtained results by these tests cannot give real activity of the sympathetic and vagal nerve, but provide the integrated function of the total autonomic reflex pathways. In order to specify the region and the magnitude of the impaired autonomic pathways, a more direct and quantitative method is required.

Pharmacological tests such as catecholamine infusion have been proposed for the evaluation of cardiovascular sensitivity [2, 3], because responsiveness of the target organ to autonomic neural discharge is an important factor modifying the cardiovascular reaction, i.e., transmitting supersensitivity from the postsynaptic damage masking decreased neural discharge, hence giving false negative findings in autonomic function tests. Although there are a few reports of pharmacological tests in children, here, we determined the reference value of alpha- and beta-adrenoceptor sensitivity [4, 5].

Serum and urinary catecholamine levels give important information of sympathetic activity, and are only the reflection of about 20% of secreted catecholamines which spill over from the synaptic clefts. A decreased plasma catecholamine level, therefore, does not directly mean decreased sympathetic outflow and should be interpreted together with organ sensitivity.

“Recent Advances in Autonomic Function Tests”

Recent advances in computer technology have made it possible to noninvasively determine fast and dynamic changes in autonomic nervous activity in humans. For example, frequency-domain analysis of heart rate variability using fast Fourier transformation and autoregressive analysis has allowed to separate low and high frequency components, which reflect vagal and sympathetic modifications of the heart.

Noninvasive continuous beat-to-beat blood pressure monitoring systems such as Finapres® (Ohmeda) and CBM-7000 (Nihon Kohin) have made it possible to detect dynamic and rapid changes in blood pressure in response to various physical and emotional stimuli. Short-term blood pressure changes mainly depend on the muscle sympathetic nervous discharge which is regulated by the baroreflex system including the high and low pressure mechanoreceptors [6]. Finapres is based on the volume clamp principle for the determination of finger arterial blood pressure as described by Penaz et al. [7] and developed by the Netherlands Research Group [8]. Clinical application of Finapres has been extensively studied [9] and was reported to be reliable except under specific conditions such as digital arterial occlusion or cold fingers [10]. Finger temperature should be standardized by keeping the hand warm during the measurement. This epoch-making apparatus has set a new stage for cardiovascular autonomic function tests in clinical practice.
Characteristics of Autonomic Function in Childhood

Autonomic function shows developmental change. Previous studies [11–13] demonstrated that children have higher vagal and lower sympathetic activity than adults and autonomic function may reach the adult level in adolescence (see below). Reference data of any autonomic function tests in adults, therefore, cannot be used in children. Moreover, autonomic function differs in different races [14], indicating that the normal reference limits should be determined for each race.

Pediatric Diseases Involving the Autonomic Nervous System

Table 1 summarizes diseases of childhood associated with organic or functional impairment of the autonomic nervous system. Among these, autonomic neuropathy involved in diabetes mellitus in conjunction with deterioration of metabolic control is a serious disorder with a potential cause of sudden death. Therefore, reliable tests which can precisely judge the progression of autonomic impairment have been utilized. Vasovagal and vasodepressor syncope, commonly seen in children and young adults, is postulated to be caused by exaggerated cardiac autonomic reflexes. Other disorders listed here were reported to have autonomic involvements. The majority of these findings were based on only one or two autonomic tests, and therefore, further investigation is needed to confirm these findings.

Autonomic Function Tests of the Cardiovascular System in Children

This article reviews current autonomic function tests which are available in pediatric practice in addition to their methodological limitation.

Table 1. Diseases affecting the autonomic nervous system in childhood

<table>
<thead>
<tr>
<th>Disease</th>
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<tbody>
<tr>
<td>Vasovagal syncope</td>
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<tr>
<td>Diabetes mellitus</td>
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<td>Reflex sympathetic dystrophy</td>
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<tr>
<td>Duchenne-type progressive muscular dystrophy</td>
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<td>Distal muscular dystrophy</td>
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<td>Familial dysautonomia</td>
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<tr>
<td>Guillain-Barré syndrome</td>
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<tr>
<td>Hyperhidrosis</td>
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<td>Children with the periodic syndrome</td>
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<tr>
<td>The adrenal insufficiency/alacrima/achalasia (3A) syndrome</td>
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<td>Fibrocalculous pancreatic diabetes</td>
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<td>Liver disease</td>
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<tr>
<td>Liver transplantation</td>
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<tr>
<td>Friedreich’s ataxia</td>
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<tr>
<td>Arnold-Chiari deformities</td>
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<tr>
<td>Raynaud’s disease</td>
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<tr>
<td>Hyperinsulinemia</td>
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<tr>
<td>Congenital heart diseases</td>
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<tr>
<td>Hypertension</td>
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<td>Peripheral nerve division</td>
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Heart Rate and Arterial Pressure Variability

Measuring the heart rate is one of the most useful applications of autonomic function. During steady state, heart rate shows small fluctuation, which reflects vagal and sympathetic interaction. Two principles have been proposed to investigate autonomic function: time-domain analysis and frequency-domain analysis. The former method is easy to perform in clinical practice and requires only a simple device to provide recordings of sequential R-R intervals of ECG or heart rate during several minutes. The measure most often used is standard deviation of R-R interval [15], but this measure only reflects the total autonomic influence on the heart beat and does not determine vagal and sympathetic activity separately.
Frequency-domain analysis including the fast Fourier transformation and the autoregressive analysis [17] allows the determination of the magnitude of power spectral density in each frequency band of heart rate variability. Many previous studies on power spectral analysis of the heart rate and arterial pressure have shown two major peaks of power density [18, 19]. One is in the low-frequency band (LF: 0.04–0.15 Hz) and the other is in the high-frequency band (HF: 0.15–0.5 Hz; fig. 1). The former is the reflection of Mayer waves of arterial pressure which is generated by the periodic discharge of the muscle sympathetic nerve. The HF peak coincides with the respiratory frequency band. The magnitude of LF of arterial pressure is considered to express muscle sympathetic nervous activity [6], while the power density of heart rate variability in LF is the reflection of sympathetic activity modified by baroreflex function including vagal pathways. Therefore, the ratio of LF and HF (LF/HF) is usually used to express sympathetic activity of the heart. HF of heart rate, on the other hand, can be used as a measure of vagal activity. In addition, the very low frequency band (0.01–0.04 Hz) has been reported to show temperature-depen-
dent heart rate fluctuation, although its significance has not been studied in children.

Power spectral analysis of heart rate has been commonly used in adults for the evaluation of cardiovascular autonomic function in heart failure [20], myocardial infarction [21], hypertension [22], syncope [23], diabetic neuropathy [24] in addition to physiological changes caused by sleep [25] and meals [26]. In contrast, there are only a few studies on power spectral analysis in children. Children with insulin-dependent diabetes mellitus (IDDM) were shown to have reduced power density of HF (vagal activity) in combination with the increment of LF/HF [27–29]. Patients with Arnold-Chiari deformities showed a decrease in LF or an increase in HF heart rate power [30], and patients with Duchenne-type progressive muscular dystrophy have an altered circadian rhythm of heart rate variability [31]. However, the methodology and the reliability of power spectral analysis have not yet been evaluated in children.

Heart rate and arterial pressure variability is strongly influenced by breathing including respiratory frequency and tidal volume, which differ in different individuals [32]. For this reason metronomically paced breathing is usually applied in adults. We determined heart rate variability using frequency-domain analysis (autoregressive analysis) in schoolchildren and adolescents, and found that uncontrolled breathing seems to be a better method since some children had difficulty to maintain adequate paced breathing during several minutes without psychological strain. As a result, 80% of the children and adolescents could have natural and relaxed breathing with a single respiratory frequency pattern in the supine position (fig. 1). Despite these methodological considerations, we found that power spectral analysis of heart rate variability could not give satisfactory results in terms of reproducibility [33], compared to that of adults [23] (coefficient of variation, 29% in children). In this study, power density of heart rate variability showed an age-related change in children and adolescents in the supine position during spontaneous breathing (fig. 2). Children from 6 to 12 years of age have higher power density in HF and lower LF/HF than adolescents (13–15 years old), suggesting that sympathetic nervous activity increases with age and vagal activity decreases inversely.

In another study of autonomic function in children with IDDM, HF power and LF/HF ratio of heart rate and arterial pressure variability did not significantly differ between IDDM patients and the controls. On the other hand, the coefficient of variation (%CV: SD/RR × 100) of heart rate and arterial pressure during uncontrolled breathing was significantly decreased in IDDM patients when
compared to controls. Therefore, heart rate variability with power spectral analysis is not the ideal autonomic function test in children and young patients with IDDM. A more simple method such as the coefficient of variation of heart rate and arterial pressure may be available in clinical practice.

**The Valsalva Maneuver**

This conventional method has been widely used for the determination of autonomic functions in various diseases in adults. Changes in blood pressure and heart rate during an induced intrathoracic pressure increase are considered to reflect sympathetic activation in the resistance vessels and sympathovagal interaction of the heart, respectively. Adult subjects usually blow into a mouthpiece which is connected to a sphygmomanometer and maintain a forced expiratory pressure of up to 40 mm Hg for 10–15 s [34].

A Valsalva index which is commonly used as a measure is calculated by the ratio of the longest R-R interval during the release phase to the shortest R-R interval during the maneuver [1]. The maneuver should be repeated several times at 3-min intervals to provide the average value.

A continuous recording of arterial pressure using a Finapres (Ohmeda) device during the maneuver can help to improve diagnostic accuracy, because attenuation of blood pressure recovery in phase II (the end of the strain) is often observed in patients with vascular sympathetic denervation (fig. 3). A baroreflex sensitivity index (BRSI) can also be obtained using Finapres as follows [35]: $\text{BRSI} = \frac{\text{the highest mean BP at overshoot (phase IV) – the lowest mean BP at release (phase III)}}{\text{the longest R-R interval at phase IV – the shortest R-R interval at phase III}}$. 

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Fig. 3. An original recording of heart rate (HR) and finger arterial pressure (BP) recording during the Valsalva maneuver in a healthy child (right panel) and children with IDDM developing blood pressure reduction (left panel). Procedure: blowing into a mouthpiece which is connected to a sphygmomanometer maintaining a forced expiratory pressure of up to 40 mm Hg for 10 s (strain).
Although there is no reported standardized method in children, we found that the breath-holding strain with the pressure level of 40 mm Hg during more than 10 s was difficult for children younger than 10 years of age [33]. As mentioned by Ringel et al. [36], the Valsalva maneuver can be omitted from the test batteries in children.

**Orthostatic Tests**

Postural change from supine position to upright posture causes a shift in blood distribution to the dependent areas and a reduction of venous return. Counteracting circulatory mechanisms controlled by the autonomic nervous system including arterial and cardiopulmonary baroreceptors are immediately activated to maintain mean arterial blood pressure with compensatory vasoconstriction in the resistance and capacitance vessels and heart rate acceleration.

Two orthostatic maneuvers have been proposed: active standing and passive head-up tilt (fig. 4). Reduction in blood pressure is reported to be larger in passive head-up tilt than in active standing probably due to more pronounced venous pooling in the lower part of the body or reduced heart rate rise during upright posture [37, 38]. Diseases involving the autonomic nervous system are associated with abnormal responses of the blood pressure and heart rate during upright posture. There was no consensus definition of orthostatic hypotension in terms of blood pressure, which is an important manifestation of autonomic failure. At the Meeting of the American Autonomic Society in 1995 [39], orthostatic hypotension was defined as a fall of more than 20 mm Hg within 3 or 4 min in either passive head-up tilt or active standing. Concurrent changes in heart rate during standing also give an important information for the diagnosis: an exaggerated increase in heart rate is found in patients with postural cachycardia syndrome, no increase in patients with hypoadrenergic orthostatic hypotension, and a decrease in patients with vasovagal attacks.

Neither standardized methods nor established criteria for orthostatic test exist in children. Table 2 summarizes recent studies on

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Fig. 4. An original recording of heart rate and finger arterial pressure during passive head-up tilt (a) and active standing in a healthy individual (b) and during active standing in a child with hyperadrenergic orthostatic hypotension (c).
orthostatic maneuvers in children with unexplained syncope of which the major origin is vasovagal. The method differs in different studies with tilt angles of 60–80 degrees and a variable period of upright posture from 10 to 60 min. Although the head-up tilt test recently has been emerging as a diagnostic tool, the positive rate of the tilt test without isoproterenol infusion does not seem to be superior to that of the active standing test in children (20–57% vs. 20–64%, respectively; table 2). Our pilot study in children with orthostatic intolerance showed almost equal occurrence of vasovagal or vasodepressor attacks in passive head-up tilt and active standing [36% (5/14) vs. 36% (5/14), respectively]. Taken together with these findings, we cannot conclude that the sensitivity of a head-up tilt test is a better method than active standing for the evaluation of unexplained syncope in children. Isoproterenol infusion which increases heart rate and more easily causes sympathoinhibitory reflexes by activating cardiac C fibers [50] is often used during orthostatic tests in order to increase sensitivity (table 3). However, Kapoor [51] recommended not to use isoproterenol infusion because of the increased false positive rate.

Active standing causes a dramatic change in blood pressure and heart rate at the onset of

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**Table 2.** Summary of results of orthostatic tests reported in children with unexplained syncope

<table>
<thead>
<tr>
<th>Researchers</th>
<th>A/P</th>
<th>Duration (min)</th>
<th>Subjects</th>
<th>Positive rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Pongiglione et al. [40]</td>
<td>A</td>
<td>10</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20 (isop)</td>
</tr>
<tr>
<td>Ross et al. [41]</td>
<td>A</td>
<td>12</td>
<td>104*</td>
<td>47</td>
</tr>
<tr>
<td>Perry and Garson [42]</td>
<td>A</td>
<td>10</td>
<td>22*</td>
<td>14</td>
</tr>
<tr>
<td>Balaji et al. [43]</td>
<td>A</td>
<td>20</td>
<td>162*</td>
<td>100</td>
</tr>
<tr>
<td>Tanaka [55]</td>
<td>A</td>
<td>10</td>
<td>34</td>
<td>10</td>
</tr>
<tr>
<td>Thilenius et al. [44]</td>
<td>P</td>
<td>60</td>
<td>35</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15 (isop)</td>
</tr>
<tr>
<td>Lerman-Sagie et al. [45]</td>
<td>P</td>
<td>60</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Grubb et al. [46]</td>
<td>P</td>
<td>30</td>
<td>30</td>
<td>6</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Fouad et al. [47]</td>
<td>P</td>
<td>20</td>
<td>44</td>
<td>25</td>
</tr>
<tr>
<td>O’Marcaigh et al. [48]</td>
<td>P</td>
<td>15</td>
<td>27*</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15 (isop)</td>
</tr>
</tbody>
</table>

Controls

| Dambrink et al. [49]      | A   | 10             | 24       | 4             |
| Fouad et al. [47]         | P   | 20             | 18       | 3             |

Positive number and rate of vasodepressor attacks during the maneuver in active (A) standing or passive head-up tilt (P) with a tilt angle indicated in parentheses. In some studies, isoproterenol infusion (+isop) was added to control study. An asterisk indicates intra-arterial cannulation.
standing: a transient but large initial drop of blood pressure and concomitant rise of heart rate [52] (fig. 4) which reversed within 30 s. These circulatory changes are postulated to reflect autonomic reflexes in the resistance vessels and the heart induced by postural change and hence translocation of blood to the lower part of the body. Wieling et al. [53] reported that beat-to-beat blood pressure and heart rate changes in the first 30 s after the onset of standing provided the necessary information for the evaluation of orthostatic disorders. In our previous study [54], we selected a new criterion of the active standing test using continuous beat-to-beat blood pressure monitoring (Finapres) for the evaluation of orthostatic intolerance in Japanese children. As mentioned above, active standing causes a large and prolonged initial drop of blood pressure in children with orthostatic intolerance including vasovagal syncope and hyperadrenergic orthostatic hypotension (fig. 4) [55]. We defined the cut off level for orthostatic intolerance: either mean blood pressure reduction in the initial stage (within 30 s after standing) of more than 60% below the basal level, or recovery time of more than 25 s or a constant fall of systolic blood pressure of more than 15% below the basal level at the stage of standing (5–10 min). Sensitivity and specificity of our criteria for diagnosis of orthostatic intolerance is 62 and 92%, respectively [55], and therefore, active standing with our new criteria (without a special tilt table) might be more useful than passive head-up tilt.

Diabetic neuropathy is a major cause of orthostatic hypotension in adults. This, however, is uncommon in children and young adults. Our previous study in IDDM showed no orthostatic hypotension, only more pronounced blood pressure responses to standing [33]. Orthostatic hypotension may develop in later stages of the disease.

**Pharmacological Tests**

Changes in heart rate and blood pressure induced by administration of adrenoceptor agonists and antagonists are considered to reflect sympathetic activity in the cardiovascular system [3]. As a representative example, a marked reduction induced by a bolus administration of phentolamine, an alpha-adrenoceptor antagonist, has been used as a diagnostic test for pheochromocytoma. Decreased catecholamine secretion from the damaged sympathetic terminal such as observed in idiopathic orthostatic hypotension increases the number of adrenoceptors in the postsynaptic membranes of the target organ, thus enhancing cardiovascular responses to a given adreno-
Tanaka’s method for pharmacological evaluation of autonomic function in the cardiovascular system. Changes in systolic blood pressure (SBP) and heart rate (HR) during the test in 1 patient. Shaded areas indicating constant infusion of each drug described in the context. Cardiac vagal activity indicating a change in HR by infusion of atropine, beta sensitivity by isoproterenol, beta tone by propranolol, alpha sensitivity: change in SBP by phenylephrine and alpha tone by phentolamine.

Misconceptor stimulant (denervation supersensitivity) [2]. When interpreting the responsiveness to these drugs, one should consider the age-related change as mentioned above.

Tanaka et al. [56] developed a pharmacological test which can determine vagal and sympathetic tone of the heart together with adrenoceptor sensitivity of the heart and the resistance vessels. In this method five different autonomic stimulants/blockers are given sequentially intravenously as shown in figure 5. Blood pressure and heart rate are monitored every 30 s. We theoretically determined that a heart rate response to atropine or propranolol infusion indicates cardiac vagal activity or beta-adrenergic tone of the heart (beta-adrenoceptor tone), respectively. Beta-adrenoceptor sensitivity (beta sensitivity) is evaluated by the increment of heart rate during the infusion of isoproterenol. On determining autonomic function of the resistance vessels, alpha-adrenergic tone (alpha tone) was assessed from the blood pressure reduction induced by a bolus infusion of phentolamine, and alpha-adrenoceptor sensitivity (alpha sensitivity) by blood pressure elevation during phenylephrine infusion. The doses of atropine, propranolol and phentolamine are reported to be able to cause complete chemical blockade of vagal and sympathetic activity in man [57]. The dose of isoproterenol or phenylephrine is adequate to cause a sufficient, but not an excessive rise in heart rate or blood pressure. The test protocol is usually completed within 40 min.

We previously reported the usefulness of this test in children with orthostatic dysregulation [4], in children with vasodepressor attacks [5], and in hypertensive children [58]. Children with orthostatic dysregulation including vasodepressor and vasovagal syncope have higher sensitivity to alpha-adrenoceptor stimulation than healthy controls with normal cardiac autonomic function, suggesting that decreased noradrenaline secretion from the sympathetic terminal in the resistance vessels is the primary cause. This is inconsistent with the study in the USA by Perry and Garson.
Fig. 6. Scattergram of intrinsic heart rate (IHR) in children and adolescents in relation with age. IHR was determined by total autonomic blockade with propranolol and atropine sulfate as described in the text.

[42], who reported higher beta-adrenoceptor sensitivity of the heart without pathological changes in sensitivity of the resistance vessels in children with vasodepressor syncope.

In contrast, hypertension caused by psychological distress in children [58] had lower adrenoceptor sensitivity of the heart and the resistance from vessels secondary to increased catecholamine secretion. Our pharmacological test may be a better method to evaluate basic sympathetic nervous tone rather than measuring serum catecholamine levels, which sometimes mislead the diagnosis of autonomic failure because of reduced clearance of noradrenaline [59].

We found a big difference of cardiovascular autonomic function between children and adults (table 3). Children had higher responses to adrenoceptor stimulation of the heart and the resistance vessels than adults, suggesting lower sympathetic nervous activity. Moreover, vagal tone, determined by complete vagal blockade by atropine, was higher in children than in adults (table 3). Intrinsic heart rate induced by complete blockade of the vagal and sympathetic nerves showed a significant negative correlation with age (fig. 6). These findings suggest that non-neuronal cardiac function such as chronotropic automaticity is higher in children than in adults, hence vagal predominance (vagotonia) is necessary to balance cardiac function.

Change in Skin Capillary Blood Flow (SBF)

The cutaneous sympathetic nervous system is mediated through cholinergic and adrenergic neurons which innervate the sweat glands and the subcutaneous blood vessels, respectively. SBF is mainly regulated at the level of arteriovenous shunts, which responds to skin sympathetic discharge. Recently SBF measured by laser Doppler flowmetry and its changes induced by various stimuli were used for the evaluation of skin sympathetic activity. For example, a 10-fold increase in SBF was detected during unilateral lumbar paravertebral sympathetic blockade in patients with reflex sympathetic dystrophy syndrome [60].

Changes in skin temperature which reflect skin blood flow were reported to be a useful autonomic test [61, 62]. Direct measurement of palm and skin temperature is a simple method, but a more precise and reliable re-
cording by infrared thermography showed high sensitivity in detecting abnormality in children and adults with peripheral neuropathy [63]. However, there are neither standardized methods nor control data available in children.

Tests for Sudomotor Activity

Stimulation of cutaneous sympathetic nerves causes excretion of sweat mediated through cholinergic neurons. Recently finger sudorometry using the capsule ventilation method or by direct measurement, sympathetic skin response, quantitative sudomotor axon reflex test with computerized digital output have been clinically applied with success in reflex sympathetic dystrophy [64], liver diseases [65], arm injuries [66], peripheral neuropathy [67], hyperhidrosis [60], etc. Bilateral measurements of the upper and lower extremities can help to identify impairment in the peripheral pathway. Further studies will be needed to determine inter- and intra-individual variation.

Intraneural Recordings of Sympathetic Activity

None of the autonomic function tests in humans mentioned above can directly determine autonomic nervous outflow. These tests can only show responsiveness of effector organs to stimuli as a result of the total integrated function of the autonomic pathway including afferents, central modification and efferent fibers. With the development of microelectrode technique, direct information can be obtained about sympathetic impulse traffic to the skin and muscle, both at rest and during various maneuvers [6]. Wallin [68] reviewed the cumulative studies on intraneural recordings of muscle and skin sympathetic activity. Muscle sympathetic nervous activity (MSNA) responsible for short-term blood pressure changes is detectable from the perineal nerve. In patients with diabetic polyneuropathy, sympathetic conduction velocity is normal as long as the fibers conduct. With sympathetic involvement in the disease, successive loss of functioning fibers leads to disappearance of detectable activity. In patients with vasovagal or vasodepressor syncope, sudden loss of sympathetic discharge was observed at the hypotensive attack [69]. There is controversy concerning the role of MSNA in the development of essential hypertension. MSNA has been studied only in adults but so far no report in children has appeared, probably because of possible complication of neuronal damage.

In conclusion, there have been only a few autonomic function tests available in children and adolescents, although recent tests using modern computer technology will be more frequently applied in pediatric practice. More sophisticated methods such as complex demodulation of heart and arterial pressure variability will be introduced [70]. No matter how the method of autonomic function tests will be advanced, it is worth noting that only a single test cannot identify the focus of impaired autonomic pathways, and thus a combination of several autonomic tests is required. Moreover, age-related changes and racial differences in autonomic function should be considered when interpreting results.
References


