Max Pulse - Reference Manual

Autonomic Nervous System Function & Blood Circulation Assessment
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1. INTRODUCTION

The Max Pulse measuring device is a simple, user-friendly, non-invasive, and painless screening device which can be used with any Windows based PC. The device provides noninvasive measurement of pulse waveform and heart rate by photoelectric plethysmography (PTG), Accelerated Plethysmography (APG), and other technologies to measure the following:

**Heart Rate Variability (HRV)** – Determines one’s overall health status and autonomic nerve system. “A recent meta-analysis of published data demonstrated that reduced cardiovascular autonomic function, as measured by heart rate variability (HRV), was strongly (i.e., relative risk is doubled) associated with increased risk of silent myocardial ischemia (lack of oxygen to the heart w/o symptoms) and mortality (DEATH).” (Department of Medicine, Manchester Royal Infirmary, Manchester, U.K.)

- **Differential Pulse Wave Index (DPI)** - Overall cardiovascular health.
- **Eccentric Constriction (EC)** – Constriction power of vessels from the left ventricle.
- **Arterial Elasticity (AE)** – Analyzes blood circulation and elasticity and resistance of the arteries.
- **Remaining Blood Volume (RBV)** – Remaining blood in the vessels after systolic contraction of the heart.
- **Wave Type** - Aging vascular health indicator.
- **Mean Heart Rate** – Average beats per minute or heart rate.
- **Arteriosclerosis Progress** – 7 pictorial wave types showing typical artery status.
- **Stress Score** – Overall stress health compared to resistance levels.
- **Stress Levels** – Mental stress, physical stress, and resistance to stress. Changes in pressure, velocity, blood volume, and other indices.

Plethysmography is a non-invasive technique for measuring the amount of blood flow present or passing through, an organ or other part of the body. Plethysmography is used to diagnose deep vein thrombosis and arterial occlusive disease.

**Pulsewave Analysis (Accelerated Plethysmography):**
Using a finger clip, the blood's pulsewave is followed from the time it leaves the heart and travels through the blood vessels down to the finger. The pulsewave is a snapshot into the cardiovascular system and evaluates arterial elasticity (arterial stiffness), which is related to atherosclerosis. Arterial stiffness is a major cardiovascular risk factor.
There is strong scientific evidence supporting the use of plethysmography as a diagnostic and prognostic tool for early warning signs of cardiovascular disease and peripheral vascular disease (including primary and secondary Raynaud's phenomenon).

**THE TEST ANALYZES:**

- Overall elasticity of large, small and peripheral arteries (arterial stiffness)
- The functional age of blood vessels
- Hydration levels
- Pulse rate
- Left ventricular ejection

The Medicore, Max Pulse scanning device is also a useful tool in assisting health-care practitioners, technicians, and individuals in the early detection of cardiovascular related issues. The test will also help assess nutraceutical and/or pharmaceutical needs. Through periodic screenings and lifestyle changes (i.e. exercise, diet, and supplementation etc.), one is able to monitor the effectiveness of these changes and how they relate to the person’s cardiovascular, autonomic and overall health status.

**2. DISCLAIMER**

For the past 20+ years, methods of the heart rate variability (HRV) analysis have become one of the most popular means of assessment of the autonomic nervous system (ANS) function because of their simple and very informative nature.

At this time there are well-defined standards and methodologies of using methods of HRV analysis, created special normative databases and criteria of assessment of various HRV parameters with regard to their comparison with normative ranges.

At the same time it is very important to point out that there is a tendency in specific cases to over exaggerate diagnostic value of the assessment of results of HRV analysis when professionals attempt to use these results to make conclusions about presence or absence of certain diseases. The Max Pulse scanning device must be used in the scope that it was intend.

This manual is aimed to outline recommendation on how to practically use this method of HRV analysis with regard to the assessment of certain aspects of the cardiovascular system and the autonomic nervous system as provided by the Max Pulse scanning device.
3. PHYSIOLOGICAL BACKGROUND

The origin of the heartbeat is located in wall of the right atrium of the heart, where a group of specialized cells form an impulse-generating tissue called the sinoatrial node or SA node. The SA node continuously generates electrical impulses. These impulses spread all over the heart muscle through specialized pathways, causing well-synchronized heart muscle contraction, leading to its proper blood pumping.

![SA Node Influencing Cardiac Wave Patterns](image)

The SA node generates around 100 – 120 heartbeats per minute at rest. However, healthy individuals have a resting heart rate (HR) that is usually much lower – around 60 – 70 beats per minute. This is due to continuous control of the autonomic nervous system (ANS) over the SA node activity.

The autonomic nervous system (ANS) is a part of our nervous system responsible for non-voluntary control of our internal organs and systems like the heart, lungs, intestines, glands, etc. ANS has its central (nuclei located in brain stem) and peripheral components (afferent and efferent fibers and peripheral ganglia) accessing all internal organs. There are two branches of the autonomic nervous system – sympathetic and parasympathetic (vagal) nervous systems that always work as antagonists in their effect on target organs.

For many organs increased stimulation of the sympathetic nervous system causes increase in their function, e.g. rising HR, increased heart stroke volume, adrenal secretion, etc. In contrast, increased stimulation of the parasympathetic nervous system inhibits their function. However for some other organs the effect of stimulation of the sympathetic and parasympathetic nervous system causes an opposed effect.
These specific effects serve our body as a very effective mechanism of survival by engaging in either stress ("fight or flight") or relaxation ("rest and digest") response.

Proper function of the autonomic nervous system is vital for maintaining the body in good health. Any stressors affecting its function can cause a regulatory imbalance in the body. Repeated and prolonged negative influence of such stressors may lead to persistent functional maladaptation and development of various health conditions.

A heart response time to the sympathetic stimulation is relatively slow. Upon stimulation of the sympathetic nervous system it takes about 5 seconds to start increasing HR and almost 30 seconds to reach its peak level. A heart response to the parasympathetic stimulation is almost instantaneous. Depending on actual phase of heart cycle, it takes just 1 or 2 heartbeats before heart slows down to its minimum level proportional to the level of stimulation.

At rest, both sympathetic and parasympathetic systems are active with moderate parasympathetic dominance. The actual balance between them is constantly changing maintaining an optimum body function.

There are various physiological factors affecting the autonomic regulation of heart rate: respiration, thermoregulation, hormonal regulation, blood pressure, cardiac output, etc. One of the most important factors is blood pressure.
There are special cells in the heart and large blood vessels that sense blood pressure level and send afferent stimulation to the central structures of the ANS. This in turn controls HR and blood vessel tonus forming a continuous feedback to maintain an optimal level of the blood pressure. This mechanism is also called baroreflex. It increases HR when blood pressure drops and vice versa and thus maintains a short-term stable blood supply to the vital organs.

One of the best ways to assess the autonomic function is to analyze minute changes in heart rate, which are caused by many factors including regulatory influence of the autonomic nervous system.

A special method of analysis can be applied to recorded heart rate readings. It is called Heart Rate Variability (HRV) analysis. The HRV analysis is a powerful, very accurate, reliable, and reproducible assessment, yet simple to perform. This will be described later in this manual.

[Figure 3] PSN and SNS Influences on Blood Pressure

Arterial baroreflex mechanism is a continuously functioning physiological regulatory system. Its goal is to maintain mean arterial blood pressure within normal range guarding its higher limit.
4. HEART RATE VARIABILITY ANALYSIS

The source information for HRV analysis is continuous beat-by-beat (not averaged) recording of heartbeat intervals. There are many ways to measure and record those intervals. However two such methods are found to be the most appropriate for this.

Pulse wave analysis is way of measuring heartbeat intervals. It is a simple and least invasive method of measurement based on photoplethysmograph (PPG). PPG is a signal reflecting changes in a blood flow in tiny blood vessels typically spotted in fingertips or earlobes. Typical PPG sensor emits infrared light towards the skin area of an earlobe or finger. The blood passing through this area through numerous tiny vessels absorbs certain portion of that light while remaining light is detected by a special photocell. The amount of absorbed light is proportional to the amount of blood passing by. Since the blood flow is not constant due to pulsations caused by heartbeats the sensor generates a very specific waveform reflecting those changes in blood flow. This waveform is usually called as a pulse wave. This waveform can be processed by a special algorithm to derive beat-by-beat heartbeat intervals.

5. HRV, ITS BACKGROUND

5.1 HEART RATE VARIABILITY (HRV), ITS DEFINITION

HRV, heart rate variability is the degree of fluctuation in the length of the intervals between heart beats. (Malik & Camm, 1995)

Heart Rate Variability (HRV) - HRV is the degree of fluctuation in the length of intervals between heart beats. They are named R - R intervals and are measured in millisecond (ms). R-R intervals are obtained from an ECG or plethysmogram. HRV measures the overall health status and autonomic nervous system (ANS) tone and balance. The ANS is composed of the sympathetic nerve system (SNS) and parasympathetic nerve system (PNS). SNS plays a role of an accelerator in our body while PNS is functioning as a brake. If one of them is broken, it will be easier to get cardiovascular diseases as ANS is not balanced. Heart rate is determined by the SA Node and ANS function. For healthy people, HRV shows complicated and irregular heart rates while unhealthy people have simple and regular heart rates. HRV has attracted much attention and has been researched in relation with various usages, conditions and diseases. HRV has been referenced in over 14,000 abstracts and papers on Pubmed. You can search the Pubmed site at:


All HRV parameters are calculated on ‘normal-to-normal’ (NN) inter-beat intervals (or NN intervals) caused by normal heart contractions paced by sinus node depolarization.
[Figure 4] R-R interval

[Figure 5] R-R intervals and their fluctuations
5.2 THE CLINICAL MEANING OF A DECREASE IN HRV (IMPORTANT to READ and UNDERSTAND)

It is found that a lowered HRV is associated with aging, decreased autonomic activity, hormonal balance, specific types of autonomic neuropathies (e.g. diabetic neuropathy) and increased risk of sudden cardiac death, after an acute heart attack.

Other research indicates that depression, panic disorders and anxiety have negative impact on autonomic function, typically causing depletion of the parasympathetic tone. On the other hand an increased sympathetic tone is associated with lowered threshold of ventricular fibrillation. These two factors could explain why such autonomic imbalance caused by significant mental and emotional stress increases risk of heart attack followed by sudden cardiac death.

Aside from that, there are multiple studies indicating that HRV is quite useful as a way to quantitatively measure physiological changes caused by various interventions both pharmacological and non-pharmacological during treatment of those conditions manifesting significant reduction in HRV. (see chart 5.3 Diseases Associated with Lowered HRV).

However, it is important to realize, that up to this point in time, the clinical implication of HRV analysis has been clearly recognized in only two medical conditions:

1. Predictor of risk of arrhythmic events or sudden cardiac death after acute heart attack
2. Clinical marker of diabetic neuropathy evolution

Nevertheless, as the number of clinical studies involving HRV in various clinical aspects and conditions grows, HRV remains one of the most promising methods of investigating general health in the future.

5.3 DISEASES ASSOCIATED WITH LOWERED HRV

- Myocardiac infarction (MI)
- Angina pectoralis
- Ventricular arrhythmia and Premature ventricular contraction (PVC)
- Sudden cardiac death
- Coronary artery disease
- Congestive heart failure
- Diabetes mellitus & Diabetic autonomic neuropathy
- Brain injury
- Epilepsy
- Multiple sclerosis
- Fibromyalgia & Chronic fatigue syndrome
- Obesity
- Guillian-Barre Syndrome
- Depression & Anxiety disorder (Panic disorder)
- Stress induced diseases
Main Clinical Application of HRV

[Figure 6] Clinical Application of HRV

MI = Myocardial Infarction, SCD = Sudden Cardiac Death, Karoshi is a Japanese term for, ‘death from over-work’.

5.4 GENERATION OF HEART RATE VARIABILITY

The intrinsic heart rate (HR) generated by the sinoatrial node (SA node) in the absence of any neural or hormonal influence is about 100 to 120 beats per minute (BPM).

However in healthy individual resting HR would never be that high. In a health individual(adult), the HR is ranging between 60 and 70 beats per minute (BPM) and the HR estimated at any given time represents the net effect of the parasympathetic (vagus) nerves, which slow HR, and the sympathetic nerves, which accelerate it.
[Figure 7] Effect of ANS on Intrinsic HR

The heart response time to sympathetic stimulation is relatively slow. It takes about 5 seconds to increase HR after the actual onset of sympathetic stimulation and almost 30 seconds to reach its peak steady level.

The heart response time to parasympathetic stimulation is almost instantaneous. Depending on the actual phase of heart cycle it takes just one or two heartbeats before the heart slows down to its minimum proportional to the level of stimulation.

The physiological origins of HRV are the fluctuations of the activity of cardiovascular vasoconstrictory and vasodilatatory centers in brain. Normally these fluctuations are a result of blood pressure oscillation (baroreflex modulated); respiration; thermoregulation and circadian biorhythm. All these factors can influence the length of beat-to-beat intervals, named R-R intervals.

The actual balance between their activities is constantly changing in attempt to achieve an optimum state, considering all internal and external stimuli. At rest, both sympathetic and parasympathetic nerves are active with the vagal effects dominant.
[Figure 8] Generation of HRV
This figure illustrates the relationships in block diagram form. The variability in HR is due to the synergistic action of the two branches of the autonomic nervous system, which acts in balance through neural, mechanical, humoral and other cardiovascular parameters, in their optimal ranges and to react optimally to changing external or internal conditions.

5.5 HISTORY OF HEART RATE VARIABILITY (HRV)

- 18th - Century Albrecht von Haller noticed heart beat not regular
- 1965 - Hon & Lee noticed that the beat to beat interval changes are the first alteration before fetal distress occurs. R-R change precedes HR change.
- 1971 - Sayers and others focused on rhythm imbedded in beat-to-beat HR
- 1977 - Wolf et al showed association of HR to sudden death post MI
- 1981 - Akselrod introduced Power Spectral Analysis (PSD)
- Late 1980’s - HRV confirmed strong predictor of mortality after an acute MI

5.6 ABOUT THE TASK FORCE

The task force was established by the Board of the European Society of Cardiology and co-sponsored by the North American Society of Pacing and Electrophysiology. Setting up the standards of measurement, physiological interpretation, and clinical use was the major goal of the task force.

The specific goals:
1. To standardize nomenclature and develop definitions of terms
2. To define physiological and pathophysiological correlations
3. To describe currently appropriate clinical applications
4. To identify areas for future research

The working fields of the members: mathematics, engineering, physiology, clinical medicine.

** The Max Pulse scanning device is designed to meet the guidelines of the task force team.

5.7 STRESS AND THE AUTONOMIC NERVOUS SYSTEM

When the body is challenged by almost anything that happens to us, from getting out of bed in the morning or running up a flight of stairs or having to stand up and give a talk, the brain activates the autonomic nervous system (ANS), the involuntary system of nerves which controls and stimulates the output of two hormones, cortisol from the adrenal cortex and epinephrine (adrenaline) from the adrenal medulla.

These two hormones and the activity of the ANS help us cope: the ANS and the epinephrine keep us alert by increasing our heart rate and blood pressure and quickly mobilizing energy reserves. In contrast, cortisol works more slowly, helps replenish energy supplies and, at the same time, helps us to remember important things. For example, cortisol readies our immune system to handle any threat -- bacterial/viral or injury.

Another aspect of cortisol action is called "containment." Many physiological systems are pitted against one another so that neither system can get out of control. The initial, first-line response too many noxious or pathogenic agents is normally "contained" by circulating levels of cortisol. This is why we take corticoids for an inflammation or skin irritation. Cortisol also contains acquired immune responses, and this is particularly useful when those responses are harmful, such as in an allergy or an autoimmune disorder.

All of these adaptive responses are described by the term "allostasis" which means "maintaining stability, or homeostasis, through change." The body actively copes with a challenge by expending energy and attempting to put things right. Most of the time it succeeds but the real problems arises when….

(1) **The systems involved in allostasis don't shut off when not needed or don't become active when they are needed.**

(2) **The balance between SNS and PNS can be disturbed and either one of the SNS or PNS can predominate over the other leading to stress related health problems.**

(3) **The body doesn't return to a state of rest after an emergency, or when the body's emergency response system is activated because the phone rings, or we look at our check book, or we have to wait in traffic.**
Depressed HRV primarily means that heart rate is monotonously regular. And it means lowered ability of the ANS’s regulatory function and ability to keep the homeostasis, cope with the internal and external stressors (stress provoking agents) and resist disease or recover in proper time.
6. METHODOLOGY OF HRV ANALYSIS

HRV can be assessed in two ways, either as a **Time Domain Analysis** or in the frequency domain as a **Power Spectral Density (PSD) analysis**. In either method, the time intervals between each successive normal QRS complex (QRS Complex corresponds to the depolarization of the right and left ventricles of the human heart) are first determined. All abnormal beats not generated by sinus node depolarizations are eliminated from the HRV analysis.

Graph B is HRV tachogram which every frequency wave from low to high frequency mixed. After filtering the high frequency power to measure the power of sole low frequency wave, only LF waves remain like in Graph C and vise versa (Graph D, remained HF wave). The technique for this analysis is called Fast Furrier Transform (FFT).

[Figure 10] Power Spectral Density Analysis & Fast Furrier Transform (FFT)
Each of the methods has advantages and disadvantages. Time domain measures are the simplest to calculate but do not provide a means to quantify autonomic balance or information on the temporal distribution (*temporal distribution: limited by time*) of power in the different branches of the autonomic nervous system. On the other hand, the main advantages of power spectral density (PSD) analysis over the time domain measures is that it supplies information on how the power is distributed (*the variance*) as a function of frequency, thereby providing a means to quantify autonomic balance at any given time.

[Figure 11] Time domain analysis and Frequency domain analysis
7. TERMINOLOGY OF HRV ANALYSIS AND DEVICE SCREEN SHOTS

7.1 BASIC TERMS

**Sinoatrial Node (SA Node)** - The SA node is the impulse-generating (pacemaker) tissue located in the right atrium of the heart, and thus the generator of normal sinus rhythm. It is a group of cells positioned on the wall of the right atrium, near the entrance of the superior vena cava. The SA node is richly innervated by parasympathetic nervous system fibers (CN X: Vagus Nerve) and by sympathetic nervous system fibers (T1-4, Spinal Nerves). This unique anatomical arrangement confers the SA node susceptible to distinctly paired and opposed autonomic influences. Stimulation of the vagus nerves (the parasympathetic fibers) causes a decrease in the SA node rate (thereby decreasing the heart rate). Parasympathetic fibers cannot change the force of contraction, however, because they only innervate the SA node and atrioventricular node (AV Node) (which control heart rate only). Stimulation via sympathetic fibers causes an increase in the SA node rate (thereby increasing the heart rate and force of contraction). Sympathetic fibers can increase the force of contraction because in addition to innervating the SA and AV nodes, they innervate the atria and ventricles themselves.

**Systolic** - When your heart beats, it contracts and pushes blood through the arteries to the rest of your body. This force creates pressure on the arteries. This is called systolic blood pressure. A normal systolic blood pressure is below 120.

A systolic blood pressure of 120 to 139 means you have prehypertension or borderline high blood pressure. Even people with prehypertension are at a higher risk of developing heart disease. A systolic blood pressure number of 140 or higher is considered to be hypertension, or high blood pressure.

**Diastolic** - The diastolic blood pressure number or the bottom number indicates the pressure in the arteries when the heart rests between beats.

A normal diastolic blood pressure number should be less than 80. A diastolic blood pressure between 80 and 89 indicates prehypertension. A diastolic blood pressure number of 90 or higher is considered to be hypertension or high blood pressure.

7.2 DIVISIONS OF THE AUTONOMIC NERVOUS SYSTEM

The autonomic system has two branches. These are called the sympathetic and the parasympathetic branches.
Sympathetic Nervous System - The sympathetic branch activates the glands and organs that defend the body against attack. It is called commonly called the 'fight-or-flight' system. Its nerves direct more blood to the muscles and the brain. The heart rate and blood pressure increase, while it decreases the blood flow to the digestive and eliminative organs.

It also activates the thyroid and adrenal glands to provide extra energy for fighting or running away. Nervousness, stress or feelings of panic are what one feels when in a sympathetic state of readiness.

The sympathetic system is catabolic, which means it tears down the body. Energy is used to prepare for defense, rather than for nourishment or for elimination of wastes. An excellent analogy is to imagine placing all of the nation’s resources in its military defense. While helpful in an emergency, if continued too long, the nation becomes much poorer for lack of productive commercial activity. The feeling of an ‘adrenalin rush’ is a product of the sympathetic system. It may feel good at first, but is always followed by a feeling of fatigue, as this system uses up energy and depletes the body.

Parasympathetic Nervous System - The parasympathetic system of nerves is concerned with nourishing, healing and regeneration of the body. It is anabolic, or concerned with rebuilding the body. Its nerves stimulate digestion, and the immune and eliminative organs. These organs include the liver, pancreas, stomach and intestines. The parasympathetic nervous system, when activated by rest, relaxation and happy thoughts, is essential for balanced living and for all healing. Moving yourself into a healthy parasympathetic state, and staying there as much of the time as possible, helps heal all health conditions, both physical and emotional ones as well.

The feeling often associated with the parasympathetic state can be one of lethargy or fatigue, as you are so relaxed. Do not, however, believe this is unhealthy. Rather, it indicates a state of repair and rebuilding in progress.

The sympathetic and parasympathetic systems are antagonistic. Either one or the other is activated most all of the time. The sympathetic system, however, always takes precedence, because it is concerned with one’s survival.

To promote balance and healing, the goal is to keep the sympathetic system turned off as much as possible. This allows the maximum healing to occur. Simple ways to do this are to rest, relax and think happy thoughts. As soon as you think fearful or angry thoughts, or become too physically active, the body shifts into a sympathetic stance.

The sympathetic nervous system may be roughly likened to the gas pedal of a car. The parasympathetic is more like the brake. Unlike a car, however, when the ‘brake’ is applied to the body, it begins to heal itself.
7.3 SCREEN SHOT #1

A. Heart Rate Monitor
B. Plethysmograph (PTG) - The “basic” wave form signal that indicates pulsation of chest wall and great arteries followed by heart beat. It measures the changes in blood volume within an organ or whole body.
C. Accelerated Plethysmograph (APG) - APG test measures the blood circulation state and aging level (state) of blood vessels in regards to vascular elasticity and hardening, through the signal at the finger tip.
D. Heart Rate Variability (HRV) Graph
E. Heart Rate Variability 'scatter' Graph
7.4 CARDIAC FUNCTION TERMS

**Differential Pulse Wave Index (DPI)** - Represents the overall health of the cardiovascular system. DPI is the main indicator that represents the aging of arteries. A lower (-) value represents an increase in vascular aging and vice versa.

**Arterial Elasticity (AE)** - Represents the blood circulation, the vascular elasticity and resistance of the vessels. It detects early cardiovascular disease like atherosclerosis and peripheral circulation dysfunction. AE analyzes the c/a value out of the basic waves [see fig. 12]. It means the elasticity of arteries and if the elasticity is bad, its value moves from (+) value to a (-) value.

**Eccentric Constriction (EC)** - Represents the contraction power of vessels from the left ventricle. EC analyzes the b/a value out of basic waves [see fig. 12]. If cardiac output is higher, the vascular state is good and the resultant value should be greater in (-) value.

**Left Ventricle** - The left ventricle receives oxygenated blood as the left atrium contracts. The blood passes through the mitral valve into the left ventricle. The aortic valve leading into the aorta is closed, allowing the ventricle to fill with blood. Once the ventricles are full, they contract. As the left ventricle contracts, the mitral valve closes and the aortic valve opens. The closure of the mitral valve prevents blood from backing into the left atrium and the opening of the aortic valve allows the blood to flow into the aorta and flow throughout the body.

**Nitric oxide** - Nitric oxide (NO), derived from the amino acid L-Arginine (ProAgri-9™), is the key endothelium-derived relaxing factor and causes vasodilation, which can help with ischemic pain, known as angina, by decreasing the cardiac workload. By dilating (expanding) the veins, nitric oxide lowers arterial pressure and left ventricular filling pressure. This vasodilation does not decrease the volume of blood the heart pumps, but rather it decreases the force the heart muscle must exert to pump the same volume of blood. **Notes:** 1. a presentation of a higher DPI with a lower EC is explained by the above paragraph. 2. C-reactive protein (CRP) inhibits endothelial nitric oxide synthase (eNOS) activity and bioactivity thus inhibiting NO production. Inhibition of eNOS by CRP offer abundant evidence that CRP has a clear role in atherothrombosis and possibly high blood pressure (Def. atherothrombosis is characterized by atherosclerotic lesion disruption with superimposed thrombus formation, is the major cause of acute coronary syndromes [ACS] and cardiovascular death. It is the leading cause of mortality in the industrialized world).

**Remaining Blood Volume (RBV)** - RBV is the remaining blood volume in the vessels after systolic contraction on the heart. If the blood vessels are healthy, there is little remaining blood volume. RBV analyzes the d/a value out of the basic waves [see fig. 12]. If the vascular state is healthy, the remaining blood volume will be lower and it describes (-) value. But, if the vascular state is poor or aging, EC will most likely be weakened and the RBV will remain high. It is an important indication of classifying the wave type.
There is an inverse relationship with DPI, EC and RBV. In a healthy vascular state, a (high-normal to optimal range) DPI and EC should correlate to lower RBV (high-normal to optimal range). In an unhealthy or aging vascular state, DPI and EC will be weaker (sub-optimal to low-normal range) and RBV will be greater (sub-optimal range to low-normal range).

7.5 SCREEN SHOT #2

A. Plethysmograph (PTG)
B. Accelerated Plethysmograph (APG)
C. Percentage of Wave Pattern Type(s)
D. Predominate Wave Type
E. Cardiac Function Chart (above – DPI, EC and AE are low with RBV increased)
F. Vessel State and Mental Stress Summary
7.6 PLETHYSMOGRAPHY AND WAVE FORM TYPES

Photoplethysmography (PPG) - Photoplethysmography is a wave form signal that indicates pulsation of chest wall and great arteries followed by heart beat, that is, the blood pressure and vascular diameter change with cardiac cycle, and these arterial pulsatile alterations propagating to peripheral vascular system mean "photoplethysmography ".

The chief aims of photoplethysmography are observation on mechanical movement of heart and kinetics of blood flow, and photoplethysmography manifests the pulsation of chest wall and great arteries followed by heart beat as wave form.

Plethysmograph (PTG) - The “basic” wave form signal that indicates pulsation of chest wall and great arteries followed by heart beat. It measures the changes in blood volume within an organ or whole body.

Accelerated Plethysmograph (APG) - APG test measures the blood circulation state and aging state of blood vessels in regards to vascular elasticity and hardening, through the signal at the finger tip. APG is also called the “final analysis” wave form. APG uses the second derivative of the waveform of the digital photoplethysmograph to stabilize the baseline and to separate components of the waveform more clearly and distinctly.

![Figure 12] Analysis of APG Wave

- a : Basal value for comparing easily in wave evaluation
- b : Initial systolic negative wave (intensity of cardiac output)
- c : Late systolic re-increased wave (vascular compliance)
- d : Late systolic re-decreased wave
### 7.7 WAVE PATTERN TYPES AND SUPPORTING DATA

<table>
<thead>
<tr>
<th>Grade</th>
<th>Progression of Arteriosclerosis</th>
<th>Wave Pattern</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wave Form 1</td>
<td>This wave type usually appears in both young, healthy individuals as well as those having good blood circulation. Even in middle age, this normal wave may be found in those who perform routine aerobic exercise.</td>
<td><img src="image1" alt="Wave Form 1" /></td>
<td><img src="image2" alt="Wave Form 1 Pattern" /></td>
</tr>
<tr>
<td>Wave Form 2</td>
<td>This wave usually appears in a person having less than ideal blood circulation, but still in a good condition. A special feature of this wave is that P2 is below the base line but above P1, and P3 is above P1. As P2, P3 are getting down, it means that a blood circulation is moving toward the poor range.</td>
<td><img src="image3" alt="Wave Form 2" /></td>
<td><img src="image4" alt="Wave Form 2 Pattern" /></td>
</tr>
<tr>
<td>Wave Form 3</td>
<td>This wave indicates that blood circulation is in the relatively bad range. A marked characteristic is that P3 is descending into the same level as P1 in contrast to wave form 2.</td>
<td><img src="image5" alt="Wave Form 3" /></td>
<td><img src="image6" alt="Wave Form 3 Pattern" /></td>
</tr>
</tbody>
</table>
  - **Symptoms:** hands and feet are getting chilled or cold. A person showing this wave type needs to start modifying their lifestyle. |
| Wave Form 4 | This wave indicates that blood circulation is dramatically reduced. A marked characteristic is that P2 is in the same level as P1, P3 in contrast to wave form 3. P1, P2 and P3 are becoming indistinguishable. | ![Wave Form 4](image7) | ![Wave Form 4 Pattern](image8) |
  - **Symptoms:** lower-leg edema, hands & feet (finger & toes) are getting chilled/cold, feeling heavy in the head or a feeling like wearing a tight hat. |
### Wave Form 5

This kind of wave appears in those individuals having very poor blood circulation. A special feature is that P3 is below P1, and if the gap is widening, it represents that blood circulation is becoming even worse.

- **Symptoms:** mild pitting ankle edema, abrupt general weakness and pain, skin color abnormality and thermo (heat/cold) anesthesia.

### Wave Form 6

This wave indicates that blood circulation is in the exceptionally bad range. A marked characteristic is that P1 and P2 are almost at the same level, and P3 is in a far lower range than P1, P2.

- **Symptoms:** Hands and feet could be blue from complications due to lack of circulation.

### Wave Form 7

This wave indicates that blood circulation is in the worst possible state. In this case, ECG often detects the abnormalities.

- **Symptoms:** This individual is liable to infection even following a slight injury (or trauma). Risks of stroke or dementia due to cerebrovascular abnormalities, this condition may not improve even though medical treatment is being administered.

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**[Figure 12] 7 Wave Pattern Types and Their Interpretation**
7.8 FREQUENCY DOMAIN ANALYSIS TERMS

**Figure 13** Frequency Domain Analysis

**Frequency Domain:** HRV is comprised of multiple frequencies. The frequency domain method analyses this waveform by looking at the different frequency components of the waveform. The two main frequency components that represent ANS activity are the low frequency (LF - sympathetic) components (0.04 to 0.15Hz) and the high frequency (HF - parasympathetic) components (0.15 to 0.4 Hz). Frequency domain measurement confirms that the LF and HF oscillatory components are relative indices of cardiac sympathetic and vagal (parasympathetic) activity respectively.

**Total Power (TP)** – Total Power is a short-term estimate of the total power, of the power spectral density, in the range of frequencies between 0 and .4 Hz. This measure reflects overall autonomic activity where sympathetic activity is the primary contributor. Total Power is calculated in milliseconds squared (ms²).

*TP combines VLF, LF and HF’s. If it is located within the I-bar or over, it means that the autonomic nervous system is functioning well. If under the I-bar, it means the autonomic nervous system is functioning poorly and that stress resistance is also weak. The clinical meaning of TP in frequency domain is similar to that of HRV.*

**Very Low Frequency (VLF)** - Very Low Frequency is a band of power spectrum range between 0.0033 and 0.04 Hz. Generally this frequency range indicates overall activity of various slow mechanisms of sympathetic function. Very Low Frequency band is calculated in milliseconds squared (ms²).
The physiological meaning of this band is most disputable. With longer time recordings, it is considered to represent sympathetic tone as well as slower hormonal and thermoregulatory effects. There are some findings indicating that in shorter recordings VLF has fair representation of various mental stress factors (negative emotions, worries, rumination etc.)

**Low Frequency (LF)** - Low Frequency is a band of power spectrum range between 0.04 and 0.15 Hz. This measure reflects both sympathetic and parasympathetic activity. Generally it is a strong indicator of sympathetic activity. Parasympathetic influence is represented by LF when respiration rate is lower than 7 breaths per minute or when taking a deep breath. Thus, when subject is in the state of relaxation with a slow and even breathing, the LF values can be very high indicating increased parasympathetic activity rather than an increase in sympathetic regulation. Low Frequency band is calculated in milliseconds squared (ms²).

*LF shows the activity of sympathetic nerve and parasympathetic nerve at the same time, but it mostly indicates the sympathetic nerve system. If it is located under the normal range, it means that he or she has lethargy, sluggishness or a possible sleep disorder.*

*Note: It’s important to educate the patient before the assessment begins, not to intentionally control breathing. For a more accurate analysis, natural breathing without any conscious respiratory manipulation is greatly desired*

**High Frequency (HF)** - High Frequency is a band of power spectrum range between 0.15 and 0.4 Hz. This band reflects parasympathetic (vagal) activity. HF is also known as a ‘respiratory’ band because it corresponds to the beat-to-beat variations caused by respiration. This phenomenon is known as Respiratory Sinus Arrhythmia (RSA). Heart rate is increased during inhalation and dropped during exhalation. High Frequency band is calculated in milliseconds squared (ms²).

This band reflects parasympathetic or vagal activity of ANS, which was confirmed after a large number of studies showed that total vagal blockade essentially eliminates the HF oscillations and reduces the power in the LF range.

Reduced PNS activity has been found in a number of cardiac pathologies due to the relationship with the electrical stability of the heart and in patients under stress or suffering from panic, anxiety or worry. Lowered PNS activity is also believed to account for much of the reduced HRV in aging.

Generally an increase in HF accompanies the increase in HRV.

*HF shows vagal activity and if it goes under the bar, it causes a lack of stability in heart function, chronic stress, functional dyspepsia, and senility.*
**LF/HF Ratio** - This is the ratio between the power of Low Frequency and High Frequency bands. This measure indicates overall balance between sympathetic and parasympathetic systems. Higher values reflect domination of the sympathetic system, while lower ones - domination of the parasympathetic system. This ratio can be used to help quantify the overall balance between the sympathetic and parasympathetic systems.

### 7.9 SCREEN SHOT #3

A. Heart Rate Chart (Average, Highest, Lowest and Irregular Heart Beats)
B. Heart Rate Variability (HRV) Graph
C. Frequency Domain Analysis and SNS and PNS Relationship Graph
D. Stress Score (0-30 Optimum, 30-50 Average, 50-80 Below-Average, 80-100 Non-Optimum)
E. Power Spectral Density
F. Physical, Mental Stress and Stress Resistance Graph
8. SET-UP STEPS AND MEASUREMENT NOTES

1. Those being screened should avoid caffeine, smoking or eating for at least 2 hours before scan.

2. Advise those to be screened, if they have acrylic nails, to remove the one covering the left index finger. This is to be done prior to the screening. Also, remove any nail polish before getting a measurement as it will cause errors as to the absorbance quantity.

3. Just prior to the scan, swab the left index finger with alcohol or acetone to remove any oils. This will facilitate for a more accurate reading and prolong the life of the probe.

4. For a more accurate scan, remove any environmental irritations such as excessive noises, vibrations, etc.

5. The temperature of a room should be kept at a comfortable level. If room temperature is too hot, peripheral vascular dilatation may occur, and if the room temperature is too cold, muscle spasm may occur. Therefore, these alterations may cause a distortion of recording results.

6. Those to be screened may need to have a few minutes to rest before getting started. Anxiousness, tension, and stress will affect the screen negatively. Everyone should be measured in resting state since the pulse-wave is affected by blood pressure, blood flow etc.

7. During the screening procedure the person should be lying flat on their back with the optical probe attached to their left index finger tip. Their arm should be kept below the level of the heart. If the optical probe location is higher than heart level, the vascular resistance in the arterial blood, evoked from heart and flowing to the periphery, would become higher in the systolic phase, and indentation or duplication wave is not clear because of small alterations of volume capacity.

Note: a seated position with the left hand resting on the left thigh is acceptable if a supine position (lying on the back) is not able to be achieved.

8. Avoid conditions that may put excessive pressure on the left arm or finger-tip.

9. Those screened should be advised to not close their eyes, fall asleep, move or talk during the screening

10. Those screened should be advised not to intentionally control breathing – breath normally.

11. In the case where the skin on the finger-tip is pigmented markedly, the absorbance quantity may rise creating the possibility in which errors may take place.

12. An individual’s follow-up screening should be performed at roughly the same time during the day as the original screening, since the HRV is known to have circadian rhythm due to changing of ANS balance (morning/evening).
9. SUPPORTING REFERENCE MATERIALS

9.1 AUTONOMIC NERVOUS SYSTEM HEALTH by Lawrence Wilson, MD
This article was originally copyrighted by the Arizona Networking News, 2005

“KEEPING YOUR AUTONOMIC SYSTEM HEALTHY”

There is much you can do to keep your autonomic system functioning well.

- **Keep your thoughts and your emotions as uplifted and positive as you possibly can, all of the time.**

- **Do your very best to stay in gratitude.** This will help keep you in a positive, uplifted state.

- **Practice forgiveness.** This places you in a position of power and compassion. It is much better than allowing yourself to feel like a victim, which always leads to a fight-or-flight response.

- **Cultivate contentment.** This is different from feeling you need to be happy all the time. Happiness, as most people know it, is often short-lived. It is often an attempt to overcome feelings of unhappiness. Contentment is a state in which you are at peace with yourself and the world, even if the world around you is not to your liking. You can learn to let the world go and choose contentment rather than attempting always to control the world.

- **Do not to compare yourself with others.** This causes fear, and often anger and resentment. The world never seems fair from our limited perspectives. There is much that is hidden. If you knew more about others' lives, you would be less anxious to trade places with them.

- **Train you mind to stay out of negative emotions. These include worry, fear, anger and guilt.** These emotions turn on the sympathetic system and keep it active. Meditation, affirmations, counseling and other natural therapies all can help. Also, surround yourself only with uplifting books, tapes and other forms of media. Pick your friends and relationships carefully. Work, school and all your activities either contribute to your contentment or detract from it.

- **Become aware of who and what truly give you energy, versus who and what mainly use up your energy.**

- **Rest often.** Nap often, and sleep at least 8 hours or more each night. The hours before midnight are by far the best for sleeping. Avoid excessive activity of any kind. Even exercise is often overdone. Exercise is a powerful sympathetic stimulant. Avoid getting exhausted by any activity you engage in. Be careful when using exercise to “run away” from stress, for example. More rest is often what is really required.
• **Practice breathing deeply.** This is one way to control the autonomic system with a voluntary action. Slow, deep breathing by itself turns off the sympathetic system.

• **Eat well.** The nervous system must be properly nourished to function correctly. Animal protein is particularly helpful for the brain and nervous system as it contains fats and proteins essential for the nerves. These include the omega-3 and omega-6 essential fatty acids. Excellent foods for the nervous system are eggs, meats, nuts, root vegetables and oily fish such as sardines and salmon.

Supplemental nutrients that calm the sympathetic system are potassium gluconate, magnesium (*transdermal or malate*), and zinc *glycinate* in particular. Most everyone should take these supplements today, as their dietary intake is often low. B-complex vitamins are also most important, and are primarily obtained from nutritional yeast, meats and eggs. High doses, however, are rarely needed. Other calming nutrients are GABA (*see below – Dopatropic*), L-taurine and L-carnitine. Herbs that calm the nervous system are valerian, passionflower, skullcap and hops, among others (*these are in Gabatone alone with 10mg’s of lithium orotate*).

“Other Nutraceuticals that may benefit here are: calcium lactate 500-1000mg’s and either, or both, Dopatropic (Biotics Research) 300mg’s before bed and Gabatone (Apex Energetics) 1 cap before bed.” Dr. Marcus Ettinger

• **Reduce your stress level as much as possible.** Stress is the main activator of the sympathetic nervous system. It can arise from within the body due to fatigue, muscle tension, spinal misalignment or nutritional deficiencies, among other reasons. Stress can also come from outside, such as financial, work or family stress. Other types of stress to minimize or avoid are living in a noisy environment, or in one with contaminated air and water.

Electromagnetic stress is also very real, although it cannot be seen. Reduce your use of computers if possible, and do not keep televisions, computers and other electrical devices on when not in use. Be sure to turn them all off when you sleep, and keep even clocks and radios away from your head in the location where you sleep. Activities like city driving and using cell phones are also stress-producing, even if you are not aware of it at the time. A simple lifestyle is much preferred.

• **Follow A Nutritional Balancing Program.** This requires a properly performed and interpreted hair tissue mineral analysis that is used to recommend diet, supplements and perhaps other detoxification procedures such as the use of an infrared sauna. The sauna is excellent for reducing excessive activity of the sympathetic nervous system and resting the adrenal and thyroid glands.
Conclusion

The health of the autonomic nervous system is an important key to healing that is often overlooked. Most people today have some degree of sympathetic nervous exhaustion. It is, in fact, a major cause of disease that should receive more attention. On a brighter note, nervous exhaustion can also cause a person to begin searching for answers deep inside. This can lead to changing your lifestyle and eating habits, and developing your inner potential. As more people become willing to change their thought patterns and lifestyles, they will experience a state of contentment and bliss that comes with having a balanced autonomic system.

9.2 METABOLIC TYPING by Beverly Nadler, CHT, CMT © 2007

SYMPATHETIC DOMINATE TYPE

Sympathetic dominant people have a stronger muscular system, heart, thyroid gland, parathyroid gland (responsible for calcium metabolism), kidneys, gonads, (ovaries or testes), uterus or prostate and adrenal medulla (the part of the adrenal gland that secretes adrenalin). The adrenal medulla is often over-active in sympathetics and they are typical “fight or flight” Type A people – “workaholic” executives, self-motivated leaders and high-pressure business people.

They have lots of nervous energy, are ambitious, enjoy exercise, love mental stimulation, have excellent powers of concentration, seem to be in constant motion and function well under stress. Sympathetics are anxious, impatient, and quick to anger and have emotional swings, but they are rarely depressed. They enjoy vegetables, fruits and sweets and have good calcium metabolism. They are slow oxidizers (meaning they digest food and burn sugar slowly) and their cells are more “acidic.” They generally thrive on vegetarian or modified vegetarian diets, with chicken, fish and just a little meat.

Sympathetic dominant people tend to be slender and pale, with big eyes. The conditions they are prone to include constipation, diabetes, digestive problems, anemia, cancer, high blood pressure, bacterial infections, non-fatal heart attacks, poor circulation, migraine headaches, insomnia, rheumatoid arthritis and hardening of the arteries. Because they are so busy, they may “forget” to eat. They tend not to “feel” sick (no time to be sick), so they don’t slow down even when they need to, which can lead to their physical and mental decline.

PARASYMPATHETIC DOMINATE TYPE

Parasympathetic dominant people have a stronger immune system, pineal gland, lungs, adrenal cortex (which secretes cortisone), spleen and digestive system -- stomach, intestines, liver, gall bladder and pancreas. They have good digestion and are fast oxidizers (meaning they digest food and burn sugar rapidly). They tend to be relaxed and easy-going, even lazy or lethargic, and don’t like to be rushed.
They are strong people with enduring energy and a high stress tolerance, unless the stress becomes too much for them and then they fall apart. They have large appetites, are usually hungry, enjoy fatty and salty foods, and don’t like to exercise.

Parasympathetics are generally slow to anger, are friendly and talkative and make great salespeople. Their body cells are alkaline, so in spite of the prevalent belief that meat is unhealthy for everyone, they need to eat meat. If they are very parasympathetic, they especially need liver and other glands. (Organic meat preferred. Kosher is second choice.)

They tend to have large frames, ruddy complexions and small eyes. The conditions parasympathetic dominant people are prone to include hypoglycemia (low blood sugar), diarrhea, overweight, low blood pressure, depression, heavy sweating and frequent urination, viral infections, allergies, asthma, cold sores, leukemia, osteoarthritis, and sexual problems (impotence in males and menstrual/menopause problems in females). If they have a heart attack, it is usually massive and kills them.

The above is a partial listing of the characteristics and tendencies of both types. Also, be aware that almost no one is purely sympathetic or parasympathetic, and that regardless of your dominance, “prone to” does not mean you will develop a specific conditions associated with your metabolic type.

BALANCED METABOLIC TYPE

In people who have a balanced autonomic nervous system, neither branch is stronger. They neither burn their food too fast or too slow, and they do equally well (or poorly, if they are sick) on all variations of foods. When they become sick, they can be prone to the conditions of either sympathetics or parasympathetics, but generally not to the extreme of either type.

It is not better or worse to have a sympathetic or parasympathetic dominant or balanced metabolism, although balanced metabolisms have more freedom in food choices. Regardless of your dominant metabolic type, you can be healthy or sick.

WHAT DETERMINES METABOLIC TYPE?

You are born that way. While it is possible to “tone down” the anxious Type A behavior that is characteristic of a sympathetic, and bring up the lethargic nature that is typical of a parasympathetic, these personality traits come with our metabolic type. They are not something we choose, anymore than we choose our height or eye color; it’s the result of genetics.

A major factor is your ethnic, nationality and ancestral background – where your ancestors came from. According to the theory, in spite of the belief that humans are “supposed” to eat foods that grow in the earth, many people cannot be healthy if they remain on a strict vegetarian diet. While the human race may have started out in “the garden of Eden” eating foods that primarily grow on trees and in the ground, as
humans migrated to areas where fruits, vegetables, nuts and seeds were not plentiful, their digestive systems either adapted to digesting what was available for food (animal meat) or they died. Their descendents (and that could be you) were born with meat-eating digestive systems. Protein from non-animal sources cannot take the place of meat (beef, lamb, game animals, and organ meats) for parasympathetic dominant people.

Since most people’s descendents came from a mixture of different backgrounds and countries and intermarried, most people (especially in America and Canada) are mixtures of metabolic types, with one predominating. Your natural (genetic) dominance can “switch” under certain conditions, such prolonged stress and illness.

9.3 AUTONOMIC IMBALANCE IN DISEASE AND NEGATIVE EMOTIONS

"Institute of Medicine (U.S.). Committee on Metabolic Monitoring for Military Field Applications"

Note: please read with a copy of Taber's Medical Dictionary handy.

There is growing evidence for the role of the autonomic nervous system (ANS) in a wide range of diseases. The ANS is generally conceived to have two major branches—the sympathetic system, associated with energy mobilization, and the parasympathetic system, associated with vegetative and restorative functions. Normally, the activity of these branches is in dynamic balance. For example, there is a well-documented circadian rhythm such that sympathetic activity is higher during daytime hours and parasympathetic activity increases at night. Other periodicities are present, and the activity of the two branches can be rapidly modulated in response to changing environmental demands.

More modern conceptions of organism function based on complexity theory hold that organism stability, adaptability, and health are maintained through variability in the dynamic relationship among system elements (Friedman and Thayer, 1998a, 1998b; Thayer and Friedman, 1997; Thayer and Lane, 2000). Thus, patterns of organized variability, rather than static levels, are preserved in the face of constantly changing environmental demands. This conception, in contrast to homeostasis, posits that the system has multiple points of stability, which necessitate a dynamic organization of resources to match specific situational demands. These demands can be conceived in terms of energy regulation such that the points of relative stability represent local energy minima required by the situation.

For example, in healthy individuals, average heart rate (HR) is greater during the day, when energy demands are higher, than at night, when energy demands are lower. Thus, the system has a local energy minimum or attractor for daytime and another for nighttime. Because the system operates “far from equilibrium,” the system is always searching for local energy minima to minimize the energy requirements of the organism. Consequentially, optimal system functioning is achieved via lability and variability in its component processes, and rigid regularity is associated with mortality, morbidity, and ill health (Lipsitz and Goldberger, 1992; Peng et al., 1994).
Another corollary of this view is that autonomic imbalance, in which one branch of the ANS dominates over the other, is associated with a lack of dynamic flexibility and health. Empirically, there is a large body of evidence to suggest that autonomic imbalance, in which typically the sympathetic system is hyperactive and the parasympathetic system is hypoactive, is associated with various pathological conditions (Malliani, Pagani, and Lombardi, 1994). In particular, when the sympathetic branch dominates for long periods of time, the energy demands on the system become excessive and ultimately cannot be met, eventuating in death. The prolonged state of alarm associated with negative emotions likewise places an excessive energy demand on the system. On the way to death, however, premature aging and disease characterize a system dominated by negative affect and autonomic imbalance.

Like many organs in the body, the heart is dually innervated. Although a wide range of physiologic factors determines HR, the ANS is the most prominent. Importantly, when both cardiac vagal (the primary parasympathetic nerve) and sympathetic inputs are blocked pharmacologically (for example, with atropine plus propranolol, the so-called double blockade), intrinsic HR is higher than the normal resting HR (Jose and Collison, 1970). This fact supports the idea that the heart is under tonic inhibitory control by parasympathetic influences. Thus, resting cardiac autonomic balance favors energy conservation by way of parasympathetic dominance over sympathetic influences. In addition, the HR time series is characterized by beat-to-beat variability over a wide range, which also implicates vagal dominance. Lowered HRV is associated with increased risk of mortality, and HRV has been proposed as a marker for disease (Task Force of the European Society of Cardiology and the North American Society of Pacing Electrophysiology, 1996).

Resting HR can be used as a rough indicator of autonomic balance, and several large studies have shown a largely linear, positive dose-response relationship between resting HR and all-cause mortality (see Habib, 1999, for review). This association was independent of gender and ethnicity, and showed a threefold increase in mortality in persons with HR over 90 beats per minute (bpm) compared to those with HRs of less than 60 bpm. It was suggested that this relationship is due to the role of HR as a major determinant of myocardial oxygen demand and the direct link of HR to the rate of myocardial energy use.

Brook and Julius (2000) have recently detailed how autonomic imbalance in the sympathetic direction is associated with a range of metabolic, hemodynamic, trophic, and rheologic (def. the phenomena of flowing matter) abnormalities that contribute to elevated cardiac morbidity and mortality. Although the relationship between HR and cardiovascular morbidity and mortality may be assumed, the fact that autonomic imbalance and HR are related to other diseases may not be as obvious. However, links do exist. For example, HRV has been shown to be associated with diabetes mellitus, and decreased HRV has been shown to precede evidence of disease provided by standard clinical tests (Ziegler, Laude, Akila, and Elgwhozi, 2001).
In addition, immune dysfunction and inflammation have been implicated in a wide range of conditions associated with aging including cardiovascular disease, diabetes, osteoporosis, arthritis, Alzheimer’s disease, periodontal disease, and certain types of cancers as well as declines in muscle strength and increased frailty and disability (Ershler and Keller, 2000; Kiecolt-Glaser et al., 2002). The common mechanism seems to involve excess proinflammatory cytokines such as interleukin 1 and 6 and tumor necrosis factor. Importantly, increased parasympathetic tone and acetylcholine (the primary parasympathetic neurotransmitter) have been shown to attenuate release of these proinflammatory cytokines, and sympathetic hyperactivity is associated with their increased production (Das, 2000; Maier and Watkins, 1998; Tracey, 2002). Thus, autonomic imbalance may be a final common pathway to increased morbidity and mortality from a host of conditions and diseases.

Although the idea is not new (Sternberg, 1997), several recent reviews have provided strong evidence linking negative affective states and dispositions to disease and ill health (Friedman and Thayer, 1998b; Kiecolt-Glaser et al., 2002; Krantz and McCeney, 2002; Musselman, Evans, and Nemeroff, 1998; Rozanski, Blumenthal, and Kaplan, 1999; Verrier and Mittleman, 2000). All of these reviews implicate altered ANS function and decreased parasympathetic activity as a possible mediator in this link.

An additional pathway between psychosocial stressors and ill health is an indirect one, in which psychosocial factors lead to poor lifestyle choices, including a lack of physical activity and the abuse of tobacco, alcohol, and drugs. Both sedentary lifestyle and substance abuse are associated with autonomic imbalance and decreased parasympathetic tone (Ingjaldsson, Laberg, and Thayer, 2003c; Nabors-Oberg, Sollers, Niaura, and Thayer, 2002; Reed, Porges, and Newlin, 1999; Rossy and Thayer, 1998; Weise, Krell, and Brinkhoff, 1986). In fact, the therapeutic effectiveness of smoking cessation, reduced alcohol consumption, and increased physical activity rest in part on their ability to restore autonomic balance and increase parasympathetic tone.

In sum, autonomic imbalance and decreased parasympathetic tone in particular may be the final common pathway linking negative affective states and dispositions, including the indirect effects via poor lifestyle, to numerous diseases and conditions associated with aging as well as increased morbidity and mortality.

**THE CENTRAL AUTONOMIC NETWORK**

Investigators have identified functional units within the central nervous system (CNS) that support goal-directed behavior and adaptability. One such entity is the central autonomic network (CAN) (Benarroch, 1993, 1997). Functionally, this network is an integrated component of an internal regulation system through which the brain controls visceromotor, neuroendocrine, and behavioral responses that are critical for goal-directed behavior, adaptability, and health.
Structurally, the CAN includes the anterior cingulate, insular, orbitofrontal, and ventromedial prefrontal cortices, the central nucleus of the amygdala, the paraventricular and related nuclei of the hypothalamus, the periaqueductal gray matter, the parabrachial nucleus, the nucleus of the solitary tract (NTS), the nucleus ambiguous, the ventrolateral medulla, the ventromedial medulla, and the medullary tegmental field.

These components are reciprocally interconnected such that information flows bidirectionally between lower and higher levels of the CNS. The primary output of the CAN is mediated through preganglionic sympathetic and parasympathetic neurons that innervate the heart via the stellate ganglia and vagus nerve, respectively. The interplay of these inputs to the cardiac sino-atrial node produces the complex variability that characterizes the HR time series (Saul, 1990). Thus, the output of the CAN is directly linked to HRV. Notably, vagal influences dominate cardiac chronotropic control (Levy, 1990). In addition, sensory information from peripheral end organs such as the heart and the immune system are fed back to the CAN. Thus, HRV is an indicator of central-peripheral neural feedback and CNS-ANS integration.

Moreover, the CAN has many features of a dynamical system. First, the components of the CAN are reciprocally interconnected, allowing for unbroken positive and negative feedback interactions and integration of autonomic responses. Second, the CAN consists of numerous parallel, distributed pathways, which permit multiple avenues to a given response. For example, a HR change of 72 to 90 bpm can be attained by various permutations of sympathetic and vagal input, including increased sympathetic or decreased vagal activity or some combination of the two, or by other processes such as circulating hormones. Moreover, within the CAN, direct and indirect paths can regulate output to preganglionic sympathetic and parasympathetic neurons. Third, CAN activity is state dependent and thus sensitive to initial conditions (see Glass and Mackey, 1988).
The CAN receives and integrates visceral, humoral, and environmental information; organizes autonomic, endocrine, and behavioral responses to environmental challenges; and is under tonic inhibitory control. This inhibition is achieved by γ-aminobutyric acid (GABA), the main inhibitory CNS neurotransmitter, emanating from interneurons within the NTS. Disruption of this pathway may lead to hypertension and sinus tachycardia, and represents a disinhibition of sympathoexcitatory circuits in the CAN (Benarroch, 1993, 1997; Masterman and Cummings, 1997; Spyer, 1989).

Other functional units within the CNS serving executive, social, affective, attentional, and motivated behavior in humans and animals have been identified (Damasio, 1998; Devinsky, Morrell, and Vogt, 1995; Masterman and Cummings, 1997; Spyer, 1989). One such network has been termed the anterior executive region (AER; Devinsky et al., 1995). The AER and its projections regulate behavior by monitoring the motivational quality of internal and external stimuli.
The AER network has been called the “rostral limbic system” and includes the anterior, insular, and orbitofrontal cortices, amygdala, periaqueductal gray, ventral striatum, and autonomic brainstem motor nuclei. Damasio (1998) has recognized a similar neural “emotion circuit” for which there is considerable structural overlap with the CAN and the AER (Thayer and Lane, 2000).

We propose that the CAN, the AER network, Damasio’s (1998) “emotion circuit,” and related systems (Masterman and Cummings, 1997; Spyer, 1989) represent a common central functional network recognized by different researchers from diverse approaches. This CNS network is associated with the processes of response organization and selection, and serves to control psychophysiological resources in attention and emotion (Friedman and Thayer, 1998a, 1998b; Thayer and Friedman, 1997). Additional structures are flexibly recruited to manage specific behavioral adaptations. This sparsely interconnected neural complex allows for maximal organism flexibility in accommodating rapidly changing environmental demands. When this network is either rigidly coupled or completely uncoupled, the ability to recruit and utilize appropriate neural support to meet a particular demand is hampered, and the organism is thus less adaptive.

AUTONOMIC REGULATION

Autonomically mediated HRV is useful as an index of neurovisceral integration and organismic self-regulation. The interaction of sympathetic and parasympathetic outputs of the CAN at the sino-atrial node produces the complex beat-to-beat variability that marks a healthy, adaptive organism. Vagal activity dominates HR control, and thus HR is under tonic inhibitory vagal control (Levy, 1990; Uijtdehaage and Thayer, 2000). HRV is also associated with prefrontal cortex activity (Lane, Reiman, Ahern, and Thayer, 2001), and the prefrontal cortex has been inversely related to subcortical activity in structures such as the amygdala that have been implicated in primitive motivation systems (Davidson, 2000).

Several lines of research point to the significance of HRV in emotions and health. Decreased HRV is linked with a number of disease states, including cardiovascular disease, diabetes, obesity, and lack of physical exercise (Stein and Kleiger, 1999). Reduced vagally mediated HRV is also associated with a number of psychological disease states, such as anxiety, depression, and hostility. For example, low HRV is consistent with the cardiac symptoms of panic anxiety as well as with its psychological expressions in poor attentional control and emotion regulation, and behavioral inflexibility (Friedman and Thayer, 1998a, 1998b). Similar reductions in HRV have been found in depression (Thayer, Smith, Rossy, Sollers, and Friedman, 1998), generalized anxiety disorder (Thayer, Friedman, and Borkovec, 1996), and posttraumatic stress disorder (Cohen, Matar, Kaplan, and Kotler, 1999). Low levels of vagal cardiovascular influence serve to disinhibit sympathoexcitatory influences. Due to differences in the temporal kinetics of the autonomic neuroeffectors, sympathetic effects on cardiac control are relatively slow (order of magnitude seconds) compared to vagal effects (order of magnitude milliseconds; see Saul, 1990).
Thus, when this rapid vagal cardiac control is low, HR cannot change as quickly in response to environmental changes. In this view, the prefrontal cortex modulates subcortical motivational circuits to serve goal-directed behavior. When the prefrontal cortex is taken “offline” for whatever reason, a relative sympathetic dominance associated with disinhibited defensive circuits is released.

Human evidence for the inhibitory role of the frontal cortex comes from a recent study of HR and HRV before and after right- and left-side intracarotid sodium amobarbital (ISA) injection (Ahern et al., 1994). HR changes were similar during each hemisphere’s pharmacological inactivation. During the 10-minute inactivations of either hemisphere, HR increased, peaked around the third minute, and gradually declined toward baseline values. These data indicate that the frontal cortex exerts tonic inhibition on brainstem sympathoexcitatory circuits. There were lateralized effects: larger and faster HR increases occurred during right-hemisphere inactivation. Moreover, vagally mediated HRV decreases were also greater in the right-hemisphere inactivations, mirroring the hemispheric effects on HR. These results support anatomical and physiological findings that right-hemispheric autonomic cardiac inputs are associated with greater chronotropic (rate) control.