**Comprehensive Pain Management Institute, LLC**
**5245 East Main Street,Columbus Ohio, 43213**

# Referral to Cardiologist/PCP

Please follow up on and evaluate/ treat the SSR/ HRV/PWV test results enclosed:

**Type 3 (Warning- Heart Weakening)**
Indicates very early signs of heart weakening. Congestive Heart Failure progresses from Type 3 down to Type 5. Patient may have slight shortness of breath, edema or fatigue.

**Type 4 (Warning Arteries Hardening)** Poor arterial health. Arteries are beginning to harden. Type 4 indicates that steps should be taken to improve arterial health.

**Type 5 (Danger - Heart Weakening)**
This wave form has been associated with more severe heart weakening. When the strength of the heart is deteriorating, patients will progress downward from a Type 3 to a Type 5. Patients normally show some symptoms such as shortness of breath, edema or fatiguing easily. Action should be taken.

**Type 6 (Danger - Arterial Hardening)**
Circulation is decreasing and hardening is severe and cause for immediate concern. Action should be taken.

**Type 7 (Severe Danger)**
Very severe hardening of the arterials warranting immediate action.

**HRV**: Normal-Abnormal_____

- **Other: Staff instructed to call PCP/ Cardiology to discuss the results**

Providers Signature:_____ Date:_____

**Leon Margolin MD, PhD/ Jing Liu CNP/ Myungsun Lipthratt CNP**

**Patient Name: -------** **INS: Caresource** **DOB: -------** **Date: 07/07/2025**

**Patient/Provider copy: R-R Interval Testing Report Addendum/Risk Factors Education Sheet.**

Medical necessity: Please review the autonomic testing clinical necessity form enclosed. In addition the patients were screened according to Autonomic Testing policy (American Academy of Neurology), Low et. Al Clinical Autonomic Disorders (2003) and Freeman R. Assessment of Cardivascular Autonomic Dysfuction (2006; 117:716-730).

In addition, the testing performed can screen for neuropathic pain (part of organic pathology assessment), assessing the heart rate variability, pulse wave analysis, stress tolerance (that can be potentially reflective of the chronic inflammatory state, as described in the attached background section) all of which is important in the treatment plan of the patient. The American Society of Addiction Medicine Handbook on Pain and Addiction stipulates that analgesics such as opioids block the experience of somatic pain. For this reason, they sometimes are referred to as anti-nociceptive agents because they block the perception of noxious (painful) information. In the case of inflammatory pain (in contrast to visceral pain or musculoskeletal pain), where inflammation is the cause of the pain, other analgesics can be used ( The American Society of Addiction Medicine Handbook on Pain and Addiction 2018, Page 37). The testing enables assessment of these conditions and providing alternative (non opioid) life style and meal choice recommendations ( see life style recommendation in the end of this hand out) that help to decrease inflammation and pain.

In contrast, neuropathic pain differs from musculoskeletal or visceral pain in that itdoes not signal injury to a bone, muscle, or organ in the body, but rather an injury to anerve cell. This distinction is important in clinical practice because traditional anti-nociceptive agents are not very effective at relieving neuropathic pain [11].Therefore, distinguishing between somatic (nociceptive) and neuropathic pain is animportant component of clinical care [1,2].

1. Dworkin RH. Recommendations for the pharmacological management of neuropathic

pain: An overview and literature update. Mayo Clin Proc. 2010;85(3Suppl):S3-S14.

2. Bennett M. The LANSS Pain Scale: The Leeds assessment of neuropathic symptoms and

signs. Pain. 2010;92:147-157.

**General Background:**

General Explanation-Heart rate, or heart pulse, is the speed of the heartbeat measured by the number of poundings of the heart per unit of time- beats per minute (bpm). The heart rate can vary according to the body's physical needs, including the need to absorb oxygen and excrete carbon dioxide. Activities that can provoke change include physical exercise, sleep, anxiety, stress, illness, and drugs.

Normal resting heart rates range from 60-100 bpm. Bradycardia is defined as a resting heart rate below 60 bpm. However, heart rates from 50 to 60 bpm are common among healthy people and do not necessarily require special attention. Tachycardia is defined as a resting heart rate above 100 bpm, though persistent rest rates between 80-100 bpm, mainly of they are present during sleep, may be signs of hyperthyroidism or anemia. Due to individuals having a constant blood volume, one of the physiological ways to deliver more oxygen to an organ is to increase heart rate permit blood to pass by the organ more often. When the heart is not beating in a regular pattern, this is referred to as an arrhythmia. These abnormalities of heart rate sometimes indicate disease. While heart rhythm is regulated entirely by the sinoatrial node under normal conditions, heart rate is regulated entirely by the sinoatrial node under normal conditions, heart rate is regulated by sympathetic and parasympathetic input to the sinoatrial node.

Scientific studies have consistently shown that autonomic nervous system function is disturbed in chronic pain patients (Bruehl and Chung, 2004). Acute pain impacts the autonomic nervous system in predictable and measureable ways as well (Koenig, 2014). This relationship between the ANS and both chronic and acute pain has important implications for the treatment and monitoring of chronic pain patients (Waldrop, 2015).An extensive interactions between the neural structures involved in pain sensation and autonomic control can be observed (Benarroch, 2001; Benarroch, 2006)." These connections provide the theoretical underpinning for the measurement of HRV in pain management settings.

R-R wave intervals and is considered the best surrogate measure of parasympathetic/sympathetic balance (Thayer, JF et al, 2008). Koenig outlined in her 2013 review paper on the topic, "The systems controlling cardiovascular function are closely coupled to systems modulating the perception of pain (Randich and Maixner, 1984) and extensive interactions between the neural structures involved in pain sensation and autonomic control can be observed (Benarroch, 2001; Benarroch, 2006)." These connections provide the theoretical underpinning for the measurement of HRV in pain management settings.

Study results suggest that patients with chronic pain also have decreased parasympathetic activity when compared to controls and that these alterations in the ANS's effects on the CV system "influence the central processing and subjective experience of pain" (Tracy, LM, et al., 2015).Reduced heart rate variability has been shown to be an independent risk factor for cardiovascular disease, therefore pain patients may have increased cardiovascular risk even in the absence of other risk factors. In patients without known cardiovascular disease, low HRV was found to increase the risk of a first CV event by 32-45% (Hillebrand, 2013).Notably, the Framingham Study found also that reduced heart rate. Heart rate variability was the only predictor of risk for sudden cardiac death (Tsuji, 1996). Later studies have also supported this finding (Makikallio, 2001).

1. The limbic system can also significantly impact heart rate related to emotional state. During periods of stress, it is not unusual to higher than normal heart rate, often accompanied by a surge in the stress hormone cortisol. Individuals experiencing extreme anxiety may manifest panic attacks with symptoms that resemble those of heart attacks. These events are typically transient and treatable. Meditation techniques have been developed to ease anxiety and have been shown to lower heart rate effectively. Doing simple deep and slow breathing exercises with one's eyes closed can also significantly reduce this anxiety and heart rate.

1. Physiological Factors Affecting Heart Rate

2. Thyroid hormones: Increased levels of the thyroid hormones (thyroxine(T4) triiodothyonine (T3)), increase the heart rate; excessive levels can trigger tachycardia. The impact of thyroid hormones is typically of a much longer duration than that of the catecholamines.

3. Calcium: Calcium ion levels greatly on heart rate and contractility; increased and of the cardiac centers an increase in both. High levels of calcium ions results in (hypercalcemia) and excessive levels can induce cardiac arrest. Drugs known as calcium channel blockers slow HR by binding to those channels and blocking or slowing the inward movement of calcium ions.

4. Caffeine and nicotine: Caffeine and nicotine are both stimulants of the nervous system and of the cardiac centers causing an increased heart rate. Caffeine works by increasing the rates of depolarization at the SA node, whereas nicotine stimulates the activity of the sympathetic neurons that deliver impulses to the heart.

The heart rate can be slowed by altered sodium and potassium levels, hypoxia (not enough oxygen), acidosis, alkalosis (abnormal blood acidity/PH), and hypernatremia (high soduim levels) may lead to tachycardia. Severely high hypernatremia may lead to fibrillation. Severe hyponatremia leads to both bradycardia and other arrhythmias.

Hypokalemia (low potassium levels) also leads to arrhythmias, whereas hyperkalemia (high potassium levels) causes the heart to become weak and flaccid, and ultimately to fail.

**R-R Interval Variability Background:**

General Explanation: Heart rate variability (R-R Interval variability) is the physiological phenomenon of variation in the time interval between heartbeats. It is measured by the variation in the beat-to-beat interval. The Framingham study proved that a decreased R-R Interval is the stimulus. The increased sympathetic tone results in a decreased R-R Interval , and the increased parasympathetic activity increases the R-R Interval .

Since R-R Interval variability reflects most directly the balance in the two branches of the Autonomic nervous system- sympathetic and parasympathetic (vagus), this triggered the creation of a new important bio – constant - the so called vegetative equilibrium. It has a wide application not only in the prevention, but also in other branches of medicine.

**Background for the use of the HRV, autonomic testing and stress index testing in chronic pain patients (based on the C.A. Waldrop MD):**

Scientific studies have consistently shown that autonomic nervous system function is disturbed in chronic pain patients (Bruehl and Chung, 2004). Acute pain also impacts the autonomic nervous system in predictable and measureable ways (Koenig, 2014). In chronic pain, the balance between the two branches of the autonomic nervous system is disturbed, such that the sympathetic branch excessively dominates over the parasympathetic, resulting in all the negative long-term effects of low HRV (Tracy, LM, Ioannou L, et al., 2016). The relationship between the autonomic nervous system and both chronic and acute pain has important implications for the complete medical treatment of chronic pain.

As Koenig outlined in his 2013 review paper on the topic, “The systems controlling cardiovascular function are closely coupled to systems modulating the perception of pain (Randich and Maixner, 1984) and extensive interactions between the neural structures involved in pain sensation and autonomic control can be observed (Benarroch, 2001; Benarroch, 2006).” Koenig further stated in his 2016 review that, “The functional interaction of these systems is an important component involved in the endogenous modulation of pain, and there is strong evidence that the functionality of these networks is altered in patients with chronic pain” (Koenig J et al, 2016). Indeed, a recent study using simultaneous HRV and fMRI showed that bodily pain does in fact induce pain- processing brainstem nuclei to function in concert with autonomic nuclei in the production of the observed cardio-vagal pain response (Sclocco R, 2016).

Koenig’s 2016 systematic review and meta-analysis, the most extensive review of the current evidence, concluded that chronic pain patients had significantly lower heart rate variability than healthy controls (Koenig J et al, 2016) and a separate experimental study the same year again confirmed this conclusion (Koenig J, Loerbroks A, 2016). Another study of 6,783 individuals published in 2018 likewise found that “beyond effects of age, sex and body mass index, the CP [chronic pain] group displayed significantly lower HRV” than the control group (Bruehl S, Olsen RB, et al., 2018).

Numerous studies have shown the relationship between HRV, as a measure the balance between the parasympathetic and sympathetic branches of the ANS, and the body’s experience of, and response to, pain. Both the sympathetic and parasympathetic nervous systems are intimately involved in the body’s pain regulation system. The balance between the two branches is disturbed in chronic pain such that the sympathetic branch excessively dominates over the parasympathetic, resulting in negative long term effects (Tracy, LM, et al., 2015).

Chronic pain, via its correlation to sympathetic dominance, is therefore associated with reduced heart rate variability. Study results suggest that patients with chronic pain also have decreased parasympathetic activity when compared to controls and that these alterations in the ANS's effects on the CV system "influence the central processing and subjective experience of pain" (Tracy, LM, et al., 2015). Notably, regions of the brain that control the autonomic nervous system and those that control pain regulation lie in close physical proximity (Bruehl and Chung, 2004).

Reduced HRV has also been reported in numerous studies on chronic pain itself, as well as in studies looking at ANS responses to acute pain. Following up on this correlation, an investigational study found that reducing pain improves heart rate variability, indicating improved ANS balance with improved pain control (Koenig, et al., 2015).

The applications of HRV measurement in pain management are many. HRV is a sensitive quantitative measure of the body's experience of pain. When used as a monitoring tool, i.e. before and after changes in medications or other treatments, HRV can act as a quantitative indicator of pain level change with treatment. HRV also has tremendous potential to help evaluate pain in patients who cannot communicate well, such as very young children and those who have suffered stroke, trauma or degenerative CNS disease.

With caution and awareness of other mitigating factors, HRV may also be used as a tool to help tease out drug seeking behavior with minimal pain or in the absence of pain, from true refractory pain. As is clearly evident, severe cardiac disease and some medications may effect HRV measurement and these must be taken in to account when evaluating a patient's level of pain using HRV. This test is another tool in the evaluation of pain and does not replace clinical judgment.

**Stress (Stress Index) and the Central Nervous System**

Numerous studies have also found that imbalance in the autonomic nervous system can help explain the wellknown link between psychological or physical stress, inflammation and the development of disease, particularly heart disease. Brosschot, Thayer and Yamamoto in their 2010 review asserted the theory of autonomic imbalance as the "final common pathway to increased morbidity and mortality from a host of conditions and diseases, including cardiovascular disease" and that this theory of autonomic imbalance may provide "a unifying framework within which to investigate the impact of risk factors, including psychosocial factors and work stress, on cardiovascular disease" (Thayer, et al., 2010). Dozens of papers including a 2013 review by Jarczok and Jarczok have shown that psychological stress reduces parasympathetic function (Jarczok MN, Jarczok M, et al. 2013).

Another review analyzing data from 11,994 patients and published in 2015, again confirmed that lower heart rate variability is directly correlated to a higher cardiovascular risk of all types and also found evidence of the connection between stress, low HRV and high cardiovascular risk (Schuster AK et 47,099 normotensive individuals and found that low heart rate variability predicted greater risk of an individual developing hypertension over the 9 years of study follow-up (Schroeder EB, 2003). al., 2015).

**Sympathetic Skin Response (SSR)**

*Introduction*

Sympathetic Skin Response (SSR) measures change of the electrical potential of the skin. The recorded skin potential

comes from the activated eccrine sweat gland. The amplitude and configuration are adjusted by sweat gland epithelium and the overlying epidermis.

Sympathetic skin response (SSR), defined as the momentary change of the electrical potential of the skin, may be spontaneous or reflexively evoked by a variety of internal or by externally applied arousal stimuli. Although the suprasegmental structures influencing the SSR in humans are not well known, SSR has been proposed as a non-invasive approach to investigate the function of the sympathetic system.

*Theoretical Background And Methods*

The first report of the galvanic skin response appeared in 1890. Since then, various terminology has been introduced on the basis of different stimulating and recording methods (e.g., electrodermal activity, sympathetic skin response [SSR], peripheral autonomic surface potential, psychogalvanic reflex, and sympathogalvanic response [SGR]). A standard method of obtaining SSR is to place a recording electrode on the palmar and plantar surfaces, because these recording sites yield higher amplitudes. A stimulator is placed on either the median or the tibial nerve of the opposite limb, and the stimulus is given randomly at a rate of less than one per minute, and with a stimulus intensity that is sufficient to cause mild pain. A 2 to 10 responses should be recorded, and SSR responses are obtainable 60% to 100% of the time in normal subjects.

Waveforms are usually triphasic, with an initial small negativity followed by a large positive wave, and a subsequent prolonged negative wave. Waveforms can also be monophasic or diphasic with an initial negative or positive peak. Maximal peak-to-peak amplitudes and mean latencies are measured. Amplitude and latency variability can be minimized by reducing stimulus frequency, increasing stimulus intensity, and/or changing stimulus site or mode. Low skin temperature, low level of attention, medication (especially anticholinergics), age, and habituation will also attenuate the response.

The SSR measures change of epidermal resistance due to sweat gland activity. The somatic afferent limb depends on the stimulus type (electrical shock, loud noise, visual threat, deep breathing); with the electrical stimulation, the afferent limb occurs via large myelinated fibers. The efferent limb is a sympathetic pathway, originating in the posterior hypothalamus, descending through the spinal cord to the intermediolateral cell column, and paravertebral ganglia and then to the sweat gland via small unmyelinated fibers.

*Clinical Utility of ESC Autonomic Testing/ Sympathetic Skin Response (SSR) Function Testing*

Illigens and Gibbons in 2009 concluded that “sudomotor abnormalities can confirm a diagnosis of autonomic dysfunction, monitor disease progression and identify success of treatment.” A 2012 study by Yajnik CS, et al. concluded that lower SMF score was significantly associated with increasing symptoms of neuropathy, increased physical abnormalities of the foot (skin changes, infection), and decreased perception of vibration and monofilament touch (Yajnik CS, et al., 2012). Likewise, Gibbons et al. concluded in 2010 that “small fiber/autonomic dysfunction has been shown to have comparable sensitivity/specificity [to the standards] for detecting neuropathy (Gibbons CH, Freeman R, Veves A, 2010). In a 2015 review article, Vinik, Nevoret and Casellini concluded that, “The unique qualities of sudomotor function tests are that, in clinical application, they may yield diagnostic information not only of autonomic dysfunction but also enhance the assessment of the small somatosensory nerves” (Vinik A, et al, 2015).

A 2014 study by Smith AG, et al. evaluated sudomotor function tests' utility in diagnosing distal symmetric polyneuropathy, another term for the peripheral polyneuropathy described above. The study recruited patients with distal symmetric polyneuropathy, or DSP, and matching controls. The researchers then examined the results of the sudomotor function test, nerve conduction studies, skin biopsy for measurement of intraepidermal nerve fiber density (IENFD), quantitative sudomotor axon reflex testing (QSART) and neuropathic scales for signs and symptoms of neuropathy. The study then directly compared the gold standard validated examination scale, the Utah Early Neuropathy Scale (UENS), with the SF and IENFD biopsy tests and found they had very similar specificity scores (67% and 63%, respectively) and that the sudomotor function testing (SMF) in fact had a higher sensitivity (77% versus 63%). The study further found that SMF scores correlated with neuropathy signs and symptoms, with sural sensory amplitude and with QSART scores.A 2019 study of 221 patients found that in patients with longer diabetes duration "abnormal handsor feet ESC had a sensitivity of 97% [and a] positive predictive value of 87% to detect neuropathy." For those with shorter duration diabetes, the sensitivity was 91% and the positive predictive value was 88%. (Carbajal-Ramirez, et al., 2019). These results again show that electrochemical skin conductance sudomotor function testing is a useful and accurate tool for detecting and monitoring distal neuropathies.

As a note, this 2014 Smith study, as well as others cited below, were performed using particular brand of electrochemical skin conductance sudomotor function test called Sudoscan. This brand's diagnostic equipment was determined by the FDA to be "substantially equivalent… to legally marketed predicate devices," under the same 510(k) code. Studies involving any brand of the equipment with the same 510(k) code are therefore evaluating the same diagnostic technology.

These are the conditions that conditions that may be associated with Small Fiber Peripheral Neuropathy(SFPN):

METABOLIC CAUSES: Diabetes mellitus, metabolic syndrome,hyperlipidemia

INHERITED CAUSES: Fabry's disease, Tangier's disease, familial amyloid polyneuropathy

TOXIC CAUSES: Chemotherapy, alcoholism, solvent exposure

AUTOIMMUNE CAUSES: Sjögren's syndrome, vasculitis/polyarteritis nodosa

AMYLOIDOSIS: Non-inherited forms of amyloidosis, e.g. lymphoma or plasma cell dyscrasias

INFECTIONS: HIV, hepatitis C, Lyme disease

IDIOPATHIC: For a relatively large percentage of cases, there is no identifiable cause of SFPN

*Diabetic Peripheral Neuropathy*

Peripheral polyneuropathy is a common and debilitating complication of diabetes, a disease often characterized by macro and micro-vascular complications (American Diabetes Association, 2009). "[Diabetic peripheral neuropathy] develops on (or with) a background of long-standing hyperglycemia, associated metabolic derangements … and cardiovascular risk factors. Alterations of microvessels, similar to those observed in diabetic retinopathy and neuropathy, appear to be associated with the pathologic alterations of nerves" (Tesfaye S, et al. 2010). Diabetic peripheral neuropathy is the earliest and most common long-term complication of diabetes mellitus (Sheshah E, et al., 2016).

Numerous studies have shown significant reduction in sweat response in diabetic patients (Provitera V, et al. 2010; Fealy RD, et al. 1989). This sudomotor dysfunction leads to dryness of skin on the foot, a factor highly associated with an increased risk of foot ulceration (Tentolouris N, et al., 2009). Foot ulceration is a highly detrimental complication of

diabetes as foot ulcerations precede approximately 84% of non-traumatic lower limb amputations in patients with diabetes (Barshes NR, et al., 2013). Diabetic peripheral neuropathy "contributes up to 78% of the risk of FU [foot ulceration]" (Sheshah E, et al., 2016). Clinicians must therefore focus on detecting DPN and sudomotor dysfunction as early as possible in order to maximize preventative strategies and avoid exacerbation of the neuropathy, foot ulceration and ultimate limb loss.

The 2016 study of 296 patients by Sheshah, et al. tested the performance of the ESC sudomotor function test against standard measures of detecting diabetic peripheral neuropathy and evaluation of the risk for foot ulceration. The study found that SMF score was highly correlated all other measure of diabetic peripheral neuropathy, such as pain sensitivity and temperature, pressure and vibration perception. The study also found that the SMF test was both sensitive (between 90.1 and 63.8% depending on the risk scale of comparison) and highly specific (85-77%) for detection of severe DPN in the feet. The test was as sensitive and specific for detection of risk of foot ulceration in that population, as well as sensitive but slightly less specific for detecting moderate foot DPN (Shesha E, et al., 2016). A 2018 study by Krieger, et al. and a 2019 study by Carbajal-Ramirez also showed the utility of ESC in early identification of peripheral neuropathy in Type 2 Diabetes.

In a study published in 2013, Cassellini, et al. evaluated the electrochemical skin conductance sudomotor function test in 376 patients including those with diabetes, diabetes with diagnosed diabetic peripheral neuropathy (DPN) and healthy controls. The study found that diabetic patients with DPN had significantly worse sudomotor function on hands and feet than patients solely diagnosed with diabetes, as well as than healthy controls. These sudomotor function scores were highly significantly correlated with the clinical Neuropathy Impairment Score – Lower Legs (NIS-LL), the somatic test Quantitative Sensory Testing (QST) and the autonomic test Quantitative Autonomic Function Testing (QAFT), all traditionally used measures of neuropathic dysfunction and resultant pain (Cassellini CM, et al., 2013). That the results of the sudomotor function tests correlate so strongly with these well-established measures supports the validity of this testing.

*Diabetic Autonomic Neuropathy*

A 2010 review by an international panel of diabetes experts defined diabetic autonomic neuropathy (DAN) as "a disorder of the autonomic nervous system in the setting of diabetes of metabolic derangements of diabetes after the exclusion of other causes. DAN may affect cardiovascular, gastrointestinal, and urogenital systems and sudomotor function. It may result in signs and symptoms or may be subclinically detectable by specific tests" (Tesfaye S, et al. 2010). If diabetic neuropathy is not diagnosed and treated appropriately it may lead to increased risk of cardiovascular disease (Vinik A, et al., 2004). Sudomotor function tests, as noted above, can detect subclinical autonomic dysfunction, thereby allowing for early diagnosis and treatment.

**Pulse Wave Velocity** (based on CA Waldrop MD)

Pulse wave velocity is the gold-standard non-invasive measurement of arterial stiffness. The test measures the velocity of the pulse wave of pressure produced in systole as it travels from the aorta to a distal point of circulation. Both the 2007 and the most recent 2013 European Society of Hypertension and European Society of Cardiology Practice Guidelines for the Management of Arterial Hypertension recommend pulse wave velocity as part of cardiovascular risk assessment (ESH and ESC, 2017). The European Society of Cardiology Working Group and the Association for Research into Arterial Structure and Physiology (ARTERY) Society likewise recommended using PWV as a biomarker to help stratify patients and prevent disease by early treatment (Vlachopoulos C, Xaplanteris P, et al., 2015).

Endes, et al, provide a brief introduction into the utility rational for using pulse wave velocity, PWV, in clinical practice, "The velocity of the pulse waves propagating along the arterial wall is a measure of stiffening of the vasculature and increased CV risk. Increased arterial stiffness was found to be independently associated with increased CV risk and CV events, as well as all-cause and CV mortality. Furthermore, arterial stiffness is an important surrogate end point of CV disease, because it reflects not only target organ damage but also pathological processes and underlying risk factors connected with vascular ageing" (Endes S, et al., 2016).

Supporting these assertions, a 2007 evidenced-based review concluded, "risk comparison demonstrated that a 1 standard deviationincrement increase in PWV is equivalent to 10 years of aging, or 1.5 to 2 times the risk of a 10 mmHgincrease in systolic blood pressure" (Khoshdel AR, et al., 2007). In a similar vein, a 2015 review found that, "A meta-analysis of cohort studies including various levels of risk has shown that a 1 m/s increase in brachial-ankle PWV is associated with a 12% increasein the risk of cardiovascular events" (Munakata M, 2014).

The Rotterdam study, an ongoing, prospective, population-based cohort study of 7983 men and women, found that "the aortic pulse wave velocity index provided additional predictive value above cardiovascular risk factors, measures of atherosclerosis, and pulse pressure" and that "aortic pulse wave velocity is an independent predictor of coronary heart disease and stroke in apparently healthy subjects" (Mattace-Raso F, et al., 2006). A 2014 individual participant meta-analysis of 17,635 subjects concluded that PWV was an independent predictor of future adverse cardiovascular events and death. The study also concluded that PWV testing improves risk classification, even after adjusting for other established cardiovascular risk factors. (Ben-Schlomo, Y, Spears M, et al., 2014)

Another individual participant data meta-analysis, done a few years after Ben-Schlomo's in 2017, and including 14,673 subjects, also found that higher PWV was significantly associated with the risk of cardiovascular disease, even when adjusted for other known CVD risk factors. This finding again established PWV as an independent predictor for the risk of CVD. The study also concluded that each standard deviation increase in the PWV was associated with a 1.19-fold increase in cardiovascular disease risk (Ohkuma, T, Ninomiya T, et al., 2017). A 2020 study by Maruhashi et al. found that baPWV was also an independent predictor of cardiovascular events (stroke, heart failure and sudden death) even in patients with hypertension who were successfully treated to a blood pressure of under 130/80.

A cohort study found "reduction in both cardiovascular and all-cause mortality in acohort study involving ESRD patients following a decrease in aortic PWV. In this study, 70% of patients with appropriateblood pressure reduction, but who maintained elevated PWV,had a reduced survival time. This evidence clearly shows thecritical deleterious role of increased stiffness and morbid arterial remodeling" (Safar ME, London GM, et al. 2004) (Khoshdel AR, et al., 2007).

Pulse wave velocity has also been shown to correlate well with other established measures of arterial stiffness. A study comparing PWV with cardiac magnetic resonance imaging (cardiac MRI) found that PWV was "well correlated with central and aortic PWV and dispensability, as measured by CMRI, regardless of age and sex" (Kim EK, Chang SA, et al., 2014). A systematic literature review of 50 studies found that "the majority of studies found increased carotid stiffness (or decreased distensibility) to be associated with carotid plaque presence, the degree of atherosclerosis, and incident stroke" (Boesen ME, et al, 2015). Likewise, a study of 654 adults in the general population compared PWV and CT scans of the coronary arteries and concluded that arterial stiffness measured by ba-PWV was highly correlated with coronary atherosclerosis (Liu, CS, et al, 2011).

*Risk Factors*

There are numerous established risk factors for increased pulse wave velocity. "Briefly, baPWV increases in patients with hypertension,diabetes, metabolic syndrome, chronic kidney disease, and sleep apnoea syndrome, as wellas in the conditions of ageing, tachycardia, and post-menopause. In hypertension and diabetes,higher baPWV is associated with more advanced organ damage. … baPWV also increases in end-stage renal disease, andhigher baPWV is associated with lower cardiac function, left ventricular hypertrophy, andseverity of carotid atherosclerosis" (Munakata M, 2015).

*PWV and Cognitive Decline*

Alvarez-Bueno's 2020 systematic review and meta-analysis found a negative association between PWV and cognition, specifically executive function, memory and global cognition, independent of "demographic, clinical and assessment characteristics." The study concludes, "These results accumulate evidence supporting that pulse-wave velocity assessment could be a useful tool to identify individuals at high risk of cognitive decline or [in the] early stages of cognitive decline, [in order] to implement interventions aimed at slowing the progression to dementia."A 2012 review of 12 studies by SW Rabkin "noted the existence of a significantassociation between increased arterial stiffness and cognitive impairment via multivariate analysis following adjustments forage, education level, and other factors that influence cognition.Moreover, the review determined that arterial stiffness is related tothe longitudinal progression of cognitive decline and that a higherPWV is a significant predictor of subsequent cognitive decline" (Rabkin SW, 2012). Li's 2017 review paper found that pulse wave velocity was related to "memory loss, poorer processing speeds, and declines in executive functioning" (Li X, Lyu P, et al., 2017).

A recent study compared cognitive performance and pulse wave velocity in patients with and without hypertension. In those with hypertension, greater arterial stiffness was associated with lower cognitive performance (Muela HCS, Costa-Hong VA, et al., 2017) In the same vein, Saij, et al conclude, "Cerebral small vessel disease (SVD) is the most common vascular cause of dementia, a major contributor to mixed dementia, and the cause of approximately one fifth of all strokes worldwide… Cerebral small vessel disease with associated arterial stiffness is a risk factor for silent cerebral lesions, stroke and cognitive impairment" (Sajj N, et al. 2016).

Li's review summarizes the data well:"Arterial stiffness is a sensitive predictor of cognitive impairment, and arterial stiffness severity has the potential to serve as an indicator used to facilitate treatments designed to prevent or delay the onset and progression of dementia in elderly individuals. Early treatment of arterial stiffness is beneficial and recommended" (Li X, Lyu P, et al., 2017).

*Future Potential and Conclusion*

Not only does PWV help determine true cardiovascular risk in patients already at risk, it also predicts the development of hypertension and cardiovascular disease in healthy patients. A Finnish study of 1449 healthy adults found that PWV measured at the beginning of the 4-year study was an independent predictor of incident hypertension at the end of the study. "An increase of 1 SD [standard deviation] inPWV was associated with a 2.75- to 2.96-mm Hg increasein systolic blood pressure measured in 2011 ($P<0.001$)" (Koivistoinen T, et al., 2018). Another study of 2835 initially healthy subjects, done within the framework of the Rotterdam study, found that the risk of developing cardiovascular disease increased with increasing pulse wave velocity. "The aortic pulse wave velocity index provided additional predictive value above cardiovascular risk factors, measures of atherosclerosis and pulse pressure." (Mattace-Raso F, et al., 2006). Pulse wave velocity may be more widely used to help identify adults at risk of developing cardiovascular disease risk factors and thus begin preventative treatments even earlier.

# Test parameters definition and relevance

Below are concise, evidence-based definitions and clinical uses for each autonomic test parameter referenced in the attached pain management report, with emphasis on their relevance to pain medicine and chronic pain management. Each summary integrates the latest references and clinical context from both the report and recent literature.

## 1. Heart Rate Variability (HRV)

**Definition:**
HRV is the variation in time intervals between consecutive heartbeats (R-R intervals), reflecting the dynamic interplay between sympathetic and parasympathetic branches of the autonomic nervous system[1][2][3].

**Clinical Use in Pain Medicine:**

- **Assessment of Autonomic Dysfunction:** Chronic pain conditions, such as fibromyalgia, neuropathic pain, and chronic back pain, are associated with reduced HRV, indicating sympathetic dominance and/or parasympathetic withdrawal[4][5][6][7][8][3].
- **Prognostic Marker:** Lower HRV is linked to increased cardiovascular risk and poor prognosis in chronic pain patients[7][3].
- **Treatment Monitoring:** HRV is used to objectively monitor the impact of pain interventions (e.g., medications, biofeedback, physical therapy, hypnosis) and to tailor individualized pain management plans[6][9][3].
- **Biofeedback:** HRV biofeedback can improve autonomic balance and reduce pain intensity[6][10][9].

**Recent Evidence:**

- HRV is validated as a non-invasive, quantitative marker for autonomic dysfunction and pain modulation[4][5][7][8][3].
- HRV changes correlate with pain intensity and treatment response in both acute and chronic pain settings[5][9][3].

## 2. Valsalva Ratio

**Definition:**
The Valsalva ratio is the maximum heart rate during the Valsalva maneuver divided by the minimum heart rate within 30 seconds after the maneuver. It is a measure of parasympathetic (vagal) function[11][12].

**Clinical Use in Pain Medicine:**

- **Autonomic Testing:** The Valsalva ratio assesses the integrity of the baroreflex and parasympathetic response, which can be impaired in chronic pain syndromes and neuropathic conditions[11][12].

- **Pain and Autonomic Dysfunction:** Abnormal Valsalva ratios may indicate insufficient autonomic compensation, often seen in patients with chronic pain, small fiber neuropathy, or complex regional pain syndrome (CRPS)[11][12][13].
- **Pain Management:** Used alongside HRV and other autonomic tests to guide diagnosis and monitor treatment effects in pain patients, especially those with suspected autonomic involvement.

**Recent Evidence:**

- The Valsalva maneuver is safe and effective for autonomic assessment and may also provide pain relief during certain procedures[14][11].
- Repeated Valsalva maneuvers can alter baroreflex indices; thus, standardized protocols are recommended for reliable results[12].

## 3. Pulse Wave Analysis (PWA) and Pulse Wave Velocity (PWV)

**Definition:**

- **PWA:** Analyzes the shape and timing of arterial pulse waves to assess arterial stiffness, central blood pressure, and vascular health[15][16].
- **PWV:** Measures the speed at which the blood pressure pulse propagates through the arterial system, serving as the gold standard for non-invasive assessment of arterial stiffness and vascular aging[17][15].

**Clinical Use in Pain Medicine:**

- **Cardiovascular Risk Assessment:** Chronic pain and associated autonomic dysfunction can accelerate vascular aging and increase arterial stiffness, both of which are captured by PWA/PWV[16][17][15].
- **Treatment Guidance:** PWA and PWV help identify patients at higher risk for cardiovascular complications, allowing for early intervention and tailored pain management strategies[16][17].
- **Monitoring Disease Progression:** Serial measurements can track the impact of pain, inflammation, and treatment interventions on vascular health[17][15].

**Recent Evidence:**

- PWV is an independent predictor of cardiovascular events and mortality, and its use is increasingly recommended for risk stratification in pain patients with comorbidities[17].
- Standardization and validation of PWV devices are critical for widespread clinical adoption[17].

## 4. Sympathetic Skin Response (SSR)

**Definition:**

SSR measures transient changes in skin electrical potential following sympathetic stimulation, reflecting the function of postganglionic sudomotor sympathetic fibers[18][19].

**Clinical Use in Pain Medicine:**

- **Diagnosis of Neuropathic Pain and CRPS:** SSR is sensitive for detecting small fiber neuropathy and autonomic dysfunction, which are common in chronic pain syndromes such as CRPS, diabetic neuropathy, and fibromyalgia[13][18][19].
- **Objective Biomarker:** SSR provides an objective measure to support clinical diagnosis, especially when symptoms are ambiguous or subjective[13][18][19].
- **Monitoring Disease and Treatment:** Changes in SSR can indicate progression or improvement of autonomic dysfunction in response to pain management interventions[18][19].

**Recent Evidence:**

- SSR is a useful adjunct in diagnosing CRPS and other pain syndromes involving autonomic dysfunction, with high sensitivity and specificity in certain populations[13][18][19].
- SSR abnormalities correlate with neuropathic pain symptoms and can help differentiate between pain subtypes[13][18][19].

## 5. R-R Interval Variability

**Definition:**

R-R interval variability is the direct measurement of the time between successive R-waves on the ECG, forming the basis for HRV analysis[2][1].

**Clinical Use in Pain Medicine:**

- **Autonomic Function Assessment:** Provides insight into the balance between sympathetic and parasympathetic nervous system activity in chronic pain patients[1][2][7].
- **Pain Modulation:** Chronic pain is associated with decreased R-R interval variability, reflecting autonomic imbalance and increased pain perception[7][3].
- **Treatment Response:** Used to monitor the effect of interventions aimed at restoring autonomic balance and reducing pain[6][10][9].

**Recent Evidence:**

- Lower R-R interval variability is associated with increased pain intensity, anxiety, and adverse cardiovascular outcomes in chronic pain populations[7][3].

## Summary Table

| Parameter | Definition & Measurement | Pain Medicine Relevance | Recent Evidence/References |
|---|---|---|---|
| **HRV** | Variation in time between heartbeats (R-R intervals) | Marker of autonomic dysfunction, pain intensity, and treatment response | [4][5][6][7][8][3] |
| **Valsalva Ratio** | Max HR during Valsalva / Min HR after maneuver | Assesses parasympathetic function, baroreflex, autonomic pain syndromes | [12][14][11] |
| **PWA/PWV** | Pulse wave shape/timing, velocity of arterial pulse | Assesses arterial stiffness, cardiovascular risk in pain patients | [16][17][15] |
| **SSR** | Skin potential change after sympathetic stimulation | Diagnoses small fiber neuropathy, CRPS, autonomic pain syndromes | [13][18][19] |
| **R-R Interval Variability** | Time between ECG R-waves, forms basis for HRV analysis | Assesses autonomic balance, pain modulation, and treatment monitoring | [1][2][7][3] |

**References include the attached report and the following key sources:**

- [4][13][17][5][14][6][11][15][18][2][10][7][8][19][9][3]

If you need detailed references or further clinical application examples for specific pain conditions, let me know.

1. Heart rate variability. Wikipedia. https://en.wikipedia.org/wiki/Heart_rate_variability. Accessed July 4, 2025.
2. RR interval. ScienceDirect. https://www.sciencedirect.com/topics/nursing-and-health-professions/rr-interval. Accessed July 4, 2025.
3. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. Front Physiol. 2017;8:495. doi:10.3389/fphys.2017.00495
4. Sgoifo A, Carnevali L, Alfonso Mde L, Amore M. Autonomic dysfunction and heart rate variability in depression. MedRxiv. Published January 8, 2025. https://www.medrxiv.org/content/10.1101/2025.01.08.25320191v1.full-text. Accessed July 4, 2025.
5. Heart rate variability: a pain management tool. GoHolistiq. https://goholistiq.com/heart-rate-variability-pain-management-tool/. Accessed July 4, 2025.
6. Heart rate variability. GoHolistiq. https://goholistiq.com/heart-rate-variability/. Accessed July 4, 2025.

7. Dantas EM, et al. Heart rate variability and pain: a systematic review. PLoS One. 2024;19(3):e0326357. doi:10.1371/journal.pone.0326357

8. Heart rate variability and pain. Front Pain Res. 2024;4:1354015. doi:10.3389/fpain.2024.1354015

9. Kim JH, et al. Heart rate variability and chronic pain: a systematic review. PubMed. 2024;39753127. https://pubmed.ncbi.nlm.nih.gov/39753127/

10. Valsalva maneuver. ScienceDirect. https://www.sciencedirect.com/topics/neuroscience/valsalva-maneuver. Accessed July 4, 2025.

11. Novak P. Autonomic disorders and pain. PMC. 2020;7272514. https://pmc.ncbi.nlm.nih.gov/articles/PMC7272514/

12. Valsalva maneuver and baroreflex. PMC. 2015;4351482. https://pmc.ncbi.nlm.nih.gov/articles/PMC4351482/

13. Gohar A, et al. Autonomic dysfunction in chronic pain. SAGE J. 2024;11297298241231903. doi:10.1177/11297298241231903

14. Pulse wave analysis measurement. Tensiomed. https://tensiomed.com/pulse-wave-analysis-measurement/. Accessed July 4, 2025.

15. Pulse wave analysis and cardiovascular risk. PMC. 2021;8031479. https://pmc.ncbi.nlm.nih.gov/articles/PMC8031479/

16. Pulse wave velocity and vascular aging. PMC. 2024;10734786. https://pmc.ncbi.nlm.nih.gov/articles/PMC10734786/

17. SSR: review of the method and its clinical use. VS Diagnostics. https://vsdiagnostics.com/wp-content/uploads/2022/01/SSR-review-of-the-method-and-its-clinical-use.pdf. Accessed July 4, 2025.

18. Shahani BT, Halperin JJ, Boulu P, Cohen J. Sympathetic skin response: a method of assessing unmyelinated axon dysfunction in peripheral neuropathies. J Neurol Neurosurg Psychiatry. 1984;47(5):536-542. doi:10.1136/jnnp.47.5.536

19. SSR and pain syndromes. PubMed. https://pubmed.ncbi.nlm.nih.gov/15253529/. Accessed July 4, 2025.

**Patient Name: -------** **INS: Caresource** **DOB: -------** **Date: 07/07/2025**

**Life Style Modifications (general suggestions, please follow the advice of your internist/family doctor):**

1. Follow up with you primary doctor and specialists on blood pressure, cholesterol levels and additional testing-Rule out hypothyroidism and electrolyte imbalance. Certain medications such as beta-blockers may lead to Bradycardia.

2. For Diabetic Patients: Please consult your primary doctor and diabetes doctor (endocrinologist) on the proper Glucose levels monitoring and diet. Intensive therapy can slow the progression and delay the appearance of abnormal autonomic dysfunction. Poor control of diabetes can make it worse.

3. **Make better meal choices by reducing/avoiding**: **refined sugars/ junk food ,** white flour, **milk from animals** with added hormones, **red meat** (beef, pork etc.) and table salts (you can review our free Youtube channel):

   **Dr Leon Margolin / Pain Relief and Qpioid Epidemic Education**

   https://www.youtube.com/watch?v=wmCYxOd8mVg

   https://www.youtube.com/watch?v=LBtpk2HrJA

   https://www.youtube.com/watch?v=N7CYUuyW9ro or other materials).

4. Keep hydrated throughout the day with pure water. Not Aquafina or Dasani or other waters that are prepared through reverse osmosis as they will strip important minerals from your body. Drink at least ½ to 1 gallon per day. Cook with pure water as well.

5. Any medications or supplement prescription from your doctor should be taken at the proper times so as to avoid swings in the amount in your body. This helps the body be more efficient, just like with food and water at regular times.

6. Establish a regular sleeping pattern and spend 10 minutes prior to sleep, doing deep breathing exercises and taking stock of the day and the next day, clearing your mind of and unnecessary burdens.

7. Make better meal choices by reducing: refined sugars, white flour, milk from animals with added hormones, and table salts. Dead sea salt or Himalayan salts are better as they do not contain aluminum which increases your condition. Eat 3-5 meals healthy meals per day at regular times and do not snack in between. Increase vegetable intake.

8. Keep hydrated throughout the day with pure water. Not Aquafina or Dasani or other waters that are prepared through reserve osmosis as they will strip important minerals from your body. Drink at least ½ to 1 gallon per day. Cook with pure water as well.

9. Regularly exercise even if it is just stretching exercises (please follow the directions of your physical therapist or exercise trainer (please let our staff if you need additional instructions on the physical therapy referral). The exercises should be sufficient to elevate your heart rate to a pace that still allows you to talk, but not sing a song.

10. Begin a weight management program with a wellness coach that can make a diet specific to your needs. **consider mindfulness program (please review the mindfulness page enclosed).** Please review the original 8 week mindfulness program book.

11. Single fiber neuropthay potential potential treatments that could include a dietary supplement containing Alpha-Lipoic Acid (600mg daily) and Benfotiamine (600mg daily). When clinically indicated, such products may be helpful to both diminish the symptoms of neuropathy, and to improve overall epidermal nerve health. Additionally, investigators have shown benefit to using combination therapy that includes L-methylfolate, methylcobalamin (**B12**) and pyridoxal 5-phosphate (**B6**).

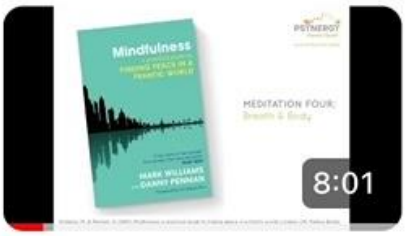
**References:** Ziegler D. Effect of 4year antioxidant treatment with alpha-lipoic acid in diabetic polyneuropathy: the NATHAN 1 trial. Diabetes 2007;56(Suppl.1):A2. Luong KV, et al.. The impact of thiamine treatmentin diabetes mellitus. J Clin Med Res 2012;4(3):153-160.

**I confirm that I read this material and all my questions were answered, I participated in an educational activity of at least 15 min duration on the life style and risk factor modifications.**

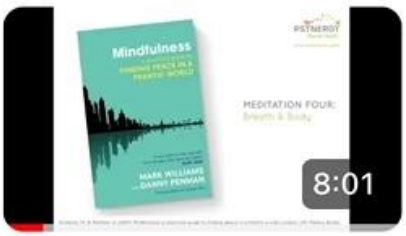
**Patient Signature**_____

2:42

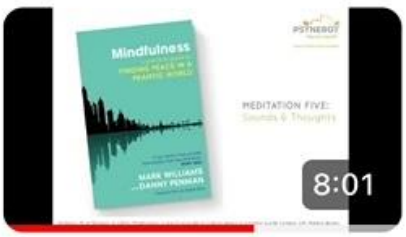
8-Week Mindfulness Co...



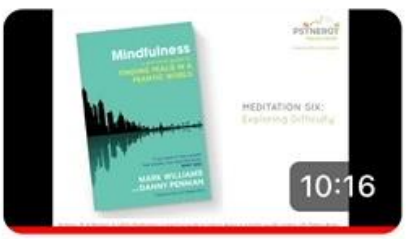

Meditation 4: Breath and body
Psynergy Mental Health
53K views • 4 years ago



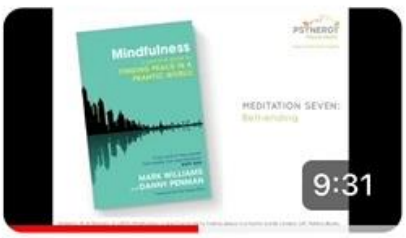

Meditation 4: Breath and body
Psynergy Mental Health
53K views • 4 years ago



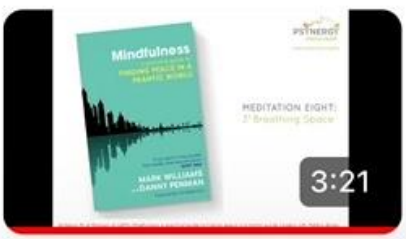

Meditation 5: Sounds and thoughts
Psynergy Mental Health
27K views • 4 years ago




Meditation 6: Exploring difficulty
Psynergy Mental Health
12K views • 4 years ago




Meditation 7: Befriending
Psynergy Mental Health
11K views • 4 years ago




Meditation 8: Three-minute breathing space
Psynergy Mental Health
16K views • 4 years ago

**R-R Interval Testing Report Addendum/Risk Factors Education Sheet.**

**Patient/Provider copy: R-R Interval Testing Report Addendum/Risk Factors Education Sheet.**

Medical necessity: Please review the autonomic testing clinical necessity form enclosed. In addition the patients were screened according to Autonomic Testing policy (American Academy of Neurology), Low et. Al Clinical Autonomic Disorders (2003) and Freeman R. Assessment of Cardivascular Autonomic Dysfuction (2006; 117:716-730).

In addition, the testing performed can screen for neuropathic pain (part of organic pathology assessment), assessing the heart rate variability, pulse wave analysis, stress tolerance (that can be potentially reflective of the chronic inflammatory state, as described in the attached background section) all of which is important in the treatment plan of the patient. The American Society of Addiction Medicine Handbook on Pain and Addiction stipulates that analgesics such as opioids block the experience of somatic pain. For this reason, they sometimes are referred to as anti-nociceptive agents because they block the perception of noxious (painful) information. In the case of inflammatory pain (in contrast to visceral pain or musculoskeletal pain), where inflammation is the cause of the pain, other analgesics can be used ( The American Society of Addiction Medicine Handbook on Pain and Addiction 2018, Page 37). The testing enables assessment of these conditions and providing alternative (non opioid) life style and meal choice recommendations ( see life style recommendation in the end of this hand out) that help to decrease inflammation and pain.

In contrast, neuropathic pain differs from musculoskeletal or visceral pain in that itdoes not signal injury to a bone, muscle, or organ in the body, but rather an injury to anerve cell. This distinction is important in clinical practice because traditional anti-nociceptive agents are not very effective at relieving neuropathic pain [11].Therefore, distinguishing between somatic (nociceptive) and neuropathic pain is animportant component of clinical care [1,2].

1. Dworkin RH. Recommendations for the pharmacological management of neuropathic

pain: An overview and literature update. Mayo Clin Proc. 2010;85(3Suppl):S3-S14.

2. Bennett M. The LANSS Pain Scale: The Leeds assessment of neuropathic symptoms and

signs. Pain. 2010;92:147-157.

**General Background:**

General Explanation-Heart rate, or heart pulse, is the speed of the heartbeat measured by the number of poundings of the heart per unit of time- beats per minute (bpm). The heart rate can vary according to the body's physical needs, including the need to absorb oxygen and excrete carbon dioxide. Activities that can provoke change include physical exercise, sleep, anxiety, stress, illness, and drugs.

Normal resting heart rates range from 60-100 bpm. Bradycardia is defined as a resting heart rate below 60 bpm. However, heart rates from 50 to 60 bpm are common among healthy people and do not necessarily require special attention. Tachycardia is defined as a resting heart rate above 100 bpm, though persistent rest rates between 80-100 bpm, mainly of they are present during sleep, may be signs of hyperthyroidism or anemia. Due to individuals having a constant blood volume, one of the physiological ways to deliver more oxygen to an organ is to increase heart rate

permit blood to pass by the organ more often. When the heart is not beating in a regular pattern, this is referred to as an arrhythmia. These abnormalities of heart rate sometimes indicate disease. While heart rhythm is regulated entirely by the sinoatrial node under normal conditions, heart rate is regulated entirely by the sinoatrial node under normal conditions, heart rate is regulated by sympathetic and parasympathetic input to the sinoatrial node.

Scientific studies have consistently shown that autonomic nervous system function is disturbed in chronic pain patients (Bruehl and Chung, 2004). Acute pain impacts the autonomic nervous system in predictable and measureable ways as well (Koenig, 2014). This relationship between the ANS and both chronic and acute pain has important implications for the treatment and monitoring of chronic pain patients (Waldrop, 2015).An extensive interactions between the neural structures involved in pain sensation and autonomic control can be observed (Benarroch, 2001; Benarroch, 2006)." These connections provide the theoretical underpinning for the measurement of HRV in pain management settings.

R-R wave intervals and is considered the best surrogate measure of parasympathetic/sympathetic balance (Thayer, JF et al, 2008). Koenig outlined in her 2013 review paper on the topic, "The systems controlling cardiovascular function are closely coupled to systems modulating the perception of pain (Randich and Maixner, 1984) and extensive interactions between the neural structures involved in pain sensation and autonomic control can be observed (Benarroch, 2001; Benarroch, 2006)." These connections provide the theoretical underpinning for the measurement of HRV in pain management settings.

Study results suggest that patients with chronic pain also have decreased parasympathetic activity when compared to controls and that these alterations in the ANS's effects on the CV system "influence the central processing and subjective experience of pain" (Tracy, LM, et al., 2015).Reduced heart rate variability has been shown to be an independent risk factor for cardiovascular disease, therefore pain patients may have increased cardiovascular risk even in the absence of other risk factors. In patients without known cardiovascular disease, low HRV was found to increase the risk of a first CV event by 32-45% (Hillebrand, 2013).Notably, the Framingham Study found also that reduced heart rate. Heart rate variability was the only predictor of risk for sudden cardiac death (Tsuji, 1996). Later studies have also supported this finding (Makikallio, 2001).

2. The limbic system can also significantly impact heart rate related to emotional state. During periods of stress, it is not unusual to higher than normal heart rate, often accompanied by a surge in the stress hormone cortisol. Individuals experiencing extreme anxiety may manifest panic attacks with symptoms that resemble those of heart attacks. These events are typically transient and treatable. Meditation techniques have been developed to ease anxiety and have been shown to lower heart rate effectively. Doing simple deep and slow breathing exercises with one's eyes closed can also significantly reduce this anxiety and heart rate.

5. Physiological Factors Affecting Heart Rate

6. Thyroid hormones: Increased levels of the thyroid hormones (thyroxine(T4) triiodothyonine (T3)), increase the heart rate; excessive levels can trigger tachycardia. The impact of thyroid hormones is typically of a much longer duration than that of the catecholamines.

7. Calcium: Calcium ion levels greatly on heart rate and contractility; increased and of the cardiac centers an increwase in both. High levels of calcium ions results in (hypercalcemia) and excessive levels can induce cardiac arrest. Drugs known as calcium channel blockers slow HR by binding to those channels and blocking or slowing the inward movement of calcium ions.

8. Caffeine and nicotine: Caffeine and nicotine are both stimulants of the nervous system and of the cardiac centers causing an increased heart rate. Caffeine works by increasing the rates of depolarization at the SA node, whereas nicotine stimulates the activity of the sympathetic neurons that deliver impulses to the heart.

The heart rate can be slowed by altered sodium and potassium levels, hypoxia (not enough oxygen), acidosis, alkalosis (abnormal blood acidity/PH), and hypernatremia (high soduim levels) may lead to tachycardia. Severely high hypernatremia may lead to fibrillation. Severe hyponatremia leads to both bradycardia and other arrhythmias. Hypokalemia (low potassium levels) also leads to arrhythmias, whereas hyperkalemia (high potassium levels) causes the heart to become weak and flaccid, and ultimately to fail.

**R-R Interval Variability Background:**

General Explanation: Heart rate variability (R-R Interval variability) is the physiological phenomenon of variation in the time interval between heartbeats. It is measured by the variation in the beat-to-beat interval. The Framingham study proved that a decreased R-R Interval is the stimulus. The increased sympathetic tone results in a decreased R-R Interval , and the increased parasympathetic activity increases the R-R Interval .

Since R-R Interval variability reflects most directly the balance in the two branches of the Autonomic nervous system- sympathetic and parasympathetic (vagus), this triggered the creation of a new important bio – constant - the so called vegetative equilibrium. It has a wide application not only in the prevention, but also in other branches of medicine.

**Background for the use of the HRV, autonomic testing and stress indextesting in chronic pain patients (based on the C.A. Waldrop MD):**

Scientific studies have consistently shown that autonomic nervous system function is disturbed in chronic pain patients (Bruehl and Chung, 2004). Acute pain also impacts the autonomic nervous system in predictable and measureable ways (Koenig, 2014). In chronic pain, the balance between the two branches of the autonomic nervous system is disturbed, such that the sympathetic branch excessively dominates over the parasympathetic, resulting in all the negative long-term effects of low HRV (Tracy, LM, Ioannou L, et al., 2016). The relationship between the autonomic nervous system and both chronic and acute pain has important implications for the complete medical treatment of chronic pain.

As Koenig outlined in his 2013 review paper on the topic, “The systems controlling cardiovascular function are closely coupled to systems modulating the perception of pain (Randich and Maixner, 1984) and extensive interactions between the neural structures involved in pain sensation and autonomic control can be observed (Benarroch, 2001; Benarroch, 2006).” Koenig further stated in his 2016 review that, “The functional interaction of these systems is an important component involved in the endogenous modulation of pain, and there is strong evidence that the functionality of these networks is altered in patients with chronic pain” (Koenig J et al, 2016). Indeed, a recent study using simultaneous HRV and fMRI showed that bodily pain does in fact induce pain- processing brainstem nuclei to function in concert with autonomic nuclei in the production of the observed cardio-vagal pain response (Sclocco R, 2016).

Koenig’s 2016 systematic review and meta-analysis, the most extensive review of the current evidence, concluded that chronic pain patients had significantly lower heart rate variability than healthy controls (Koenig J et al, 2016) and a separate experimental study the same year again confirmed this conclusion (Koenig J, Loerbroks A, 2016). Another study of 6,783 individuals published in 2018 likewise found that “beyond effects of age, sex and body mass index, the CP [chronic pain] group displayed significantly lower HRV” than the control group (Bruehl S, Olsen RB, et al., 2018).

Numerous studies have shown the relationship between HRV, as a measure the balance between the parasympathetic and sympathetic branches of the ANS, and the body's experience of, and response to, pain. Both the sympathetic and parasympathetic nervous systems are intimately involved in the body's pain regulation system. The balance between the two branches is disturbed in chronic pain such that the sympathetic branch excessively dominates over the parasympathetic, resulting in negative long term effects (Tracy, LM, et al., 2015).

Chronic pain, via its correlation to sympathetic dominance, is therefore associated with reduced heart rate variability. Study results suggest that patients with chronic pain also have decreased parasympathetic activity when compared to controls and that these alterations in the ANS's effects on the CV system "influence the central processing and subjective experience of pain" (Tracy, LM, et al., 2015). Notably, regions of the brain that control the autonomic nervous system and those that control pain regulation lie in close physical proximity (Bruehl and Chung, 2004).

Reduced HRV has also been reported in numerous studies on chronic pain itself, as well as in studies looking at ANS responses to acute pain. Following up on this correlation, an investigational study found that reducing pain improves heart rate variability, indicating improved ANS balance with improved pain control (Koenig, et al., 2015).

The applications of HRV measurement in pain management are many. HRV is a sensitive quantitative measure of the body's experience of pain. When used as a monitoring tool, i.e. before and after changes in medications or other treatments, HRV can act as a quantitative indicator of pain level change with treatment. HRV also has tremendous potential to help evaluate pain in patients who cannot communicate well, such as very young children and those who have suffered stroke, trauma or degenerative CNS disease.

With caution and awareness of other mitigating factors, HRV may also be used as a tool to help tease out drug seeking behavior with minimal pain or in the absence of pain, from true refractory pain. As is clearly evident, severe cardiac disease and some medications may effect HRV measurement and these must be taken in to account when evaluating a patient's level of pain using HRV. This test is another tool in the evaluation of pain and does not replace clinical judgment.

**Stress (Stress Index) and the Central Nervous System**

Numerous studies have also found that imbalance in the autonomic nervous system can help explain the wellknown link between psychological or physical stress, inflammation and the development of disease, particularly heart disease. Brosschot, Thayer and Yamamoto in their 2010 review asserted the theory of autonomic imbalance as the "final common pathway to increased morbidity and mortality from a host of conditions and diseases, including cardiovascular disease" and that this theory of autonomic imbalance may provide "a unifying framework within which to investigate the impact of risk factors, including psychosocial factors and work stress, on cardiovascular disease" (Thayer, et al., 2010). Dozens of papers including a 2013 review by Jarczok and Jarczok have shown that psychological stress reduces parasympathetic function (Jarczok MN, Jarczok M, et al. 2013).

Another review analyzing data from 11,994 patients and published in 2015, again confirmed that lower heart rate variability is directly correlated to a higher cardiovascular risk of all types and also found evidence of the connection between stress, low HRV and high cardiovascular risk (Schuster AK et 47,099 normotensive individuals and found that low heart rate variability predicted greater risk of an individual developing hypertension over the 9 years of study follow-up (Schroeder EB, 2003). al., 2015).

**Patient Name: -------** **INS: Caresource** **DOB: -------** **Date: 07/07/2025**

**Life Style Modifications (general suggestions, please follow the advice of your internist/family doctor):**

1. Follow up with you primary doctor and specialists on blood pressure, cholesterol levels and additional testing-Rule out hypothyroidism and electrolyte imbalance. Certain medications such as beta-blockers may lead to Bradycardia.

2. For Diabetic Patients: Please consult your primary doctor and diabetes doctor (endocrinologist) on the proper Glucose levels monitoring and diet. Intensive therapy can slow the progression and delay the appearance of abnormal autonomic dysfunction. Poor control of diabetes can make it worse.

3. **Make better meal choices by reducing/avoiding**: **refined sugars/ junk food ,** white flour, **milk from animals** with added hormones, **red meat** (beef, pork etc.) and table salts (you can review our free Youtube channel):

   **Dr Leon Margolin / Pain Relief and Qpioid Epidemic Education**

   https://www.youtube.com/watch?v=wmCYxOd8mVg

   https://www.youtube.com/watch?v=LBtpk2HrJA

   https://www.youtube.com/watch?v=N7CYUuyW9ro or other materials).

4. Keep hydrated throughout the day with pure water. Not Aquafina or Dasani or other waters that are prepared through reverse osmosis as they will strip important minerals from your body. Drink at least ½ to 1 gallon per day. Cook with pure water as well.

5. Any medications or supplement prescription from your doctor should be taken at the proper times so as to avoid swings in the amount in your body. This helps the body be more efficient, just like with food and water at regular times.

6. Establish a regular sleeping pattern and spend 10 minutes prior to sleep, doing deep breathing exercises and taking stock of the day and the next day, clearing your mind of and unnecessary burdens.

7. Make better meal choices by reducing: refined sugars, white flour, milk from animals with added hormones, and table salts. Dead sea salt or Himalayan salts are better as they do not contain aluminum which increases your condition. Eat 3-5 meals healthy meals per day at regular times and do not snack in between. Increase vegetable intake.

8. Keep hydrated throughout the day with pure water. Not Aquafina or Dasani or other waters that are prepared through reserve osmosis as they will strip important minerals from your body. Drink at least ½ to 1 gallon per day. Cook with pure water as well.

9. Regularly exercise even if it is just stretching exercises (please follow the directions of your physical therapist or exercise trainer (please let our staff if you need additional instructions on the physical therapy referral). The exercises should be sufficient to elevate your heart rate to a pace that still allows you to talk, but not sing a song.

10. Begin a weight management program with a wellness coach that can make a diet specific to your needs; **consider mindfulness program (please review the mindfulness page enclosed).** Please review the original 8 week mindfulness program book.

11. Single fiber neuropthay potential potential treatments that could include a dietary supplement containing Alpha-Lipoic Acid (600mg daily) and Benfotiamine (600mg daily). When clinically indicated, such products may be helpful to both diminish the symptoms of neuropathy, and to improve overall epidermal nerve health. Additionally, investigators have shown benefit to using combination therapy that includes L-methylfolate, methylcobalamin (**B12**) and pyridoxal 5-phosphate (**B6**).

**References:** Ziegler D. Effect of 4year antioxidant treatment with alpha-lipoic acid in diabetic polyneuropathy: the NATHAN 1 trial. Diabetes 2007;56(Suppl.1):A2. Luong KV, et al.. The impact of thiamine treatmentin diabetes mellitus. J Clin Med Res 2012;4(3):153-160.

**I confirm that I read this material and all my questions were answered, I participated in an educational activity of at least 15 min duration on the life style and risk factor modifications.**

**Patient Signature**_____

**Patient Name: -------** **INS: Caresource** **DOB: -------** **Date: 07/07/2025**

# Dietary Recommendations for Osteoarthritis, Degenerative Disk Disease, Neuropathy, and Decreased Heart Rate Variability

## Core Principles

- Emphasize a whole food, plant-based or Mediterranean-style diet rich in anti-inflammatory and antioxidant nutrients.
- Target foods that support joint, nerve,and cardiovascular health while minimizing inflammation and oxidative stress.

## Osteoarthritis & Degenerative Disk Disease

**Recommended Foods:**

- Fruits and Vegetables: Especially leafy greens, berries, and cruciferous vegetables for antioxidants and polyphenols.
- Legumes: Beans, chickpeas, and lentils reduce inflammation and may slow joint degeneration.
- Whole Grains: Oats, brown rice, and quinoa provide fiber and micronutrients.
- Nuts and Seeds: Walnuts, flaxseed, and chia for omega-3 fatty acids, which are anti- inflammatory.
- Spices: Turmeric and ginger have natural anti-inflammatory properties.

**Foods to Limit/Avoid:**

- Processed meats, red meat, and foods high in saturated/trans fats.
- Refined grains and added sugars.
- Excess sodium and ultra-processed foods.

## Neuropathy

**Recommended Foods:**

- B-vitamins: Whole grains, legumes, nuts, and seeds support nerve health.
- Omega-3 fatty acids: Flaxseed, chia, walnuts, and fatty fish (if not strictly plant-based).
- Magnesium-rich foods: Leafy greens, beans, nuts, and seeds.
- Antioxidant-rich foods: Berries, citrus, and colorful vegetables.

**Foods to Limit/Avoid:**

- Alcohol and foods high in added sugars or saturated fat, which can worsen nerve damage.

**Decreased Heart Rate Variability (HRV)**

**Recommended Foods and Practices:**

- Plant-Based Diet: Associated with better HRV, lower blood pressure, and improved vagal tone [1] [2].
- Leafy Greens: Even half a serving a day may significantly reduce heart attack risk and improve HRV [1].
- Mediterranean Diet: Algae based omega 3, olive oil, nuts, vegetables, and whole grains increase HRV and lower cardiac risk [3] [4].
- Omega-3 Fatty Acids: From nuts, seeds, and algae based omega 3, shown to improve HRV and cardiac electrical stability [3] [4].
- Beans and Legumes: Daily intake can lower resting heart rate as much as significant exercise [2] [5].
- B-Vitamins and Polyphenols: Found in whole grains, nuts, and colorful fruits, these nutrients support HRV [3] [4].

**Foods to Limit/Avoid:**

- High intakes of saturated/trans fats and high-glycemic carbohydrates reduce HRV[3]
- Alcohol: Even moderate regular intake can lower HRV[4]
- Processed foods and excess sodium.

**Lifestyle Tips**

- Exercise: Regular aerobic activity (150–300 minutes/week) improves HRV and joint health[1 [4]
- Slow Breathing/Meditation: Practices like slow-paced breathing (about 6 breaths/minute) can improve HRV [1].
- Sleep Hygiene: Good sleep supports HRV and nerve/joint health[4].
- Weight Management: Maintaining a healthy weight reduces joint and nerve stress.

**Summary Table**

| Condition | Recommended Foods & Practices | Foods to Limit/Avoid |
|---|---|---|
| Osteoarthritis & DDD | Leafy greens, berries, legumes, turmeric, nuts | Red/processed meat, refined grains |
| Neuropathy | B-vitamin foods, omega-3s, magnesium, antioxidants | Alcohol, saturated fats, added sugars |
| Low HRV | Plant-based/Mediterranean diet, beans, leafy greens, omega-3s, exercise, slow breathing | Processed foods, saturated/trans fats, alcohol |

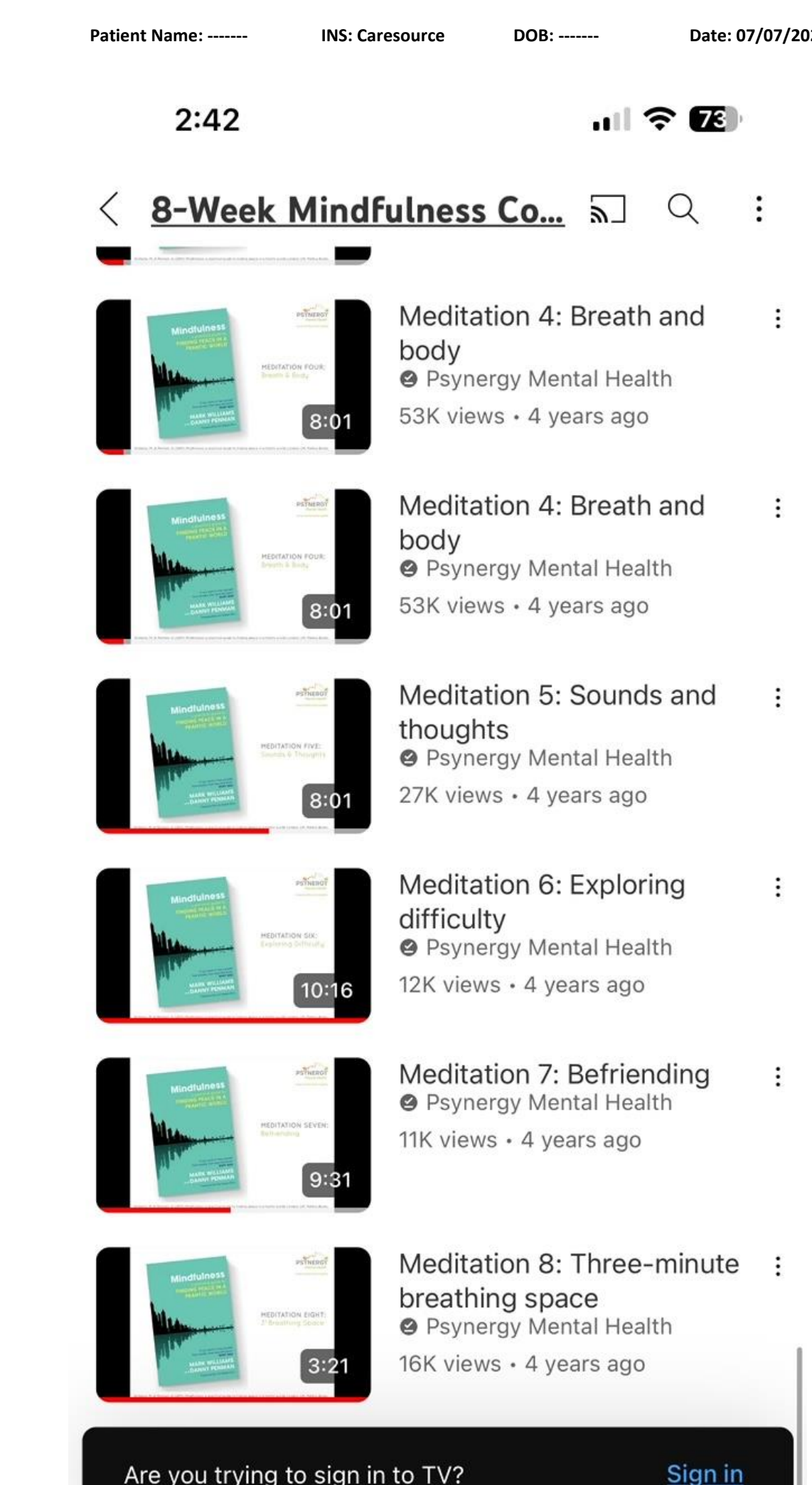
**Key Takeaways**

- A diet high in plant-based foods, legumes, leafy greens, nuts, and omega-3s is beneficial across all these conditions [1] [3] [4] [2] [5].
- Limit animal products, processed foods, unhealthy fats, and alcohol.
- Regular exercise, slow breathing, and good sleep further support heart, nerve, and joint health [1] [4].

**References:**

NutritionFacts.org, published literature,and Physicians Committee for Responsible Medicine [1] [3] [4] [2] [5] [6].

1. https://nutritionfacts.org/video/how-to-improve-your-heart-rate-variability/
2. https://nutritionfacts.org/topics/heart-rate/
3. https://pmc.ncbi.nlm.nih.gov/articles/PMC5882295/
4. https://www.healthcent ral.com/condition/heart-disease/how-to-improve-heart-rate-variability-hrv
5. https://nutritionfacts.org/blog/the-best-food-to-slowing-your-resting-heart-rate/
6. work.nutrition_research


2:42
8-Week Mindfulness Co...
Meditation 4: Breath and body
Psynergy Mental Health
53K views • 4 years ago
8:01
Meditation 4: Breath and body
Psynergy Mental Health
53K views • 4 years ago
8:01
Meditation 5: Sounds and thoughts
Psynergy Mental Health
27K views • 4 years ago
8:01
Meditation 6: Exploring difficulty
Psynergy Mental Health
12K views • 4 years ago
10:16
Meditation 7: Befriending
Psynergy Mental Health
11K views • 4 years ago
9:31
Meditation 8: Three-minute breathing space
Psynergy Mental Health
16K views • 4 years ago
3:21
Are you trying to sign in to TV?
Sign in

**Patient Name: -------** **INS: Caresource** **DOB: -------** **Date: 07/07/2025**

**Initial/Follow up Autonomic and R-R Interval Variability / Valsalva Ratio Testing Report**

The patient participated for at least 3-6 months in the program that included opioid and alternative medications, minimally invasive procedures (i.e. peripheral nerve blocks), patient was evaluated by pain psychology.

Retesting Autonomic and R-R variability studies indicated based on the enclosed Pre-Qualification Questionnaire (offered on the retesting) and the symptoms indicated in the SOAP note, prior records and enclosed assessments. The testing ordered to identify risk and impact of the patient symptoms on the cardiac and autonomic nervous system to determine appropriate treatment plan in compliance with the patient contract, consent for treatment and guidelines for opioid medication use enclosed. We may consider retesting in the future to monitor compliance, effectiveness of treatments and stability of the cardiovascular system.

Autonomic study was performed in the upper and low extremities (protocol based on Electrodiagnostic Medicine 2nd edition, Daniel Dimitru et al. p. 252-253, Manual for Nerve Conduction Study 4thedition, p. 134 - 136). Joseph Colombo et al. p. 275-291 Clinical Autonomic Dysfunction and El-Badawy et al. "Sympathetic Dysfunction in Patients with Chronic Low Back Pain and Failed Back Surgery Syndrome" Clin J Pain Vol. 32, #3, March 2016. Additional studies performed using Pulse Wave Velocity technique, please find separate reports enclosed.

**Autonomic Study Interpretation:**

Temperature _____

**Normal values:**

**Latency hand 1.5 / leg 2.0** **Amplitude hand/ leg 2.7 / 1.2**

The autonomic study:

❑ was normal

❑ was inconclusive, no response (NR) UE / LE / Right / Left / BL

❑ showed abnormal latency / amplitude.

❑ There was a significant difference in the latency / amplitude between the hand and the foot.

❑ There was a significant difference in the latency / amplitude between the right side and the left side.

**Patient Name: -------** **INS: Caresource** **DOB: -------** **Date: 07/07/2025**

## R-R Interval Variability / Valsalva Ratio testing

SDRR Normal Values (based on Urooj et al. International Journal of Pharmacy and Pharmaceutical Sciences Vol. 3, Issue 1, 2011).Additional testing was performed while patient was positioned in a head tilt position using tilt table. Additional studies performed using Pulse Wave Velocity technique, please find separate reports enclosed.

Decreased SSDR is associated with higher cardiovascular risk:

❑ Patient was not able to stop or modify relevant medications at this time. Results were possibly attenuated by medications (i.e. beta blockers, tricyclics).

**Normal Subject: 53.39-64.3** **Hypertensive: 44.4-53.9** **Smoker: 40.3-52.1**

**SDRR testing results are consistent with:**

□ Decreased; Mild / Moderate/ Severe cardiovascular risk

□ Not decreased

**Valsalva Ratio Normal Values (Based on Phillip A. Low et al. , Clinical Autonomic Disorders)**

| **Parameter** | | **20 years** | | **40 years** | | **60 years** | | **80 years** | |
|---|---|---|---|---|---|---|---|---|---|
| 2.5-97.5% | | Male | Female | Male | Female | Male | Female | Male | Female |
| | **Min** | 1.50 | 1.41 | 1.36 | 1.47 | 1.21 | 1.36 | 1.21 | 1.36 |
| | **Max** | 2.97 | 2.97 | 2.60 | 2.88 | 2.88 | 2.65 | 2.23 | 2.60 |

**Valsalva Ratio** is:

□ Within the range 2.5%-97.5% of the normal values

□ Below the 2.5% of the range of suggestive of insufficient sympathetic response compensation

□ Above the 97.5% of the range of suggestive of insufficient parasympathetic response compensation

**Assessment and plan:**

The results of the study discussed with the patient.

❑ **These findings are usually seen with a small fiber neuropathy. The abnormal results discussed with the patient.**

❑**We discussed the conditions that may be associated with Small Fiber Peripheral Neuropathy(SFPN):**

METABOLIC CAUSES: Diabetes mellitus, metabolic syndrome,hyperlipidemia

INHERITED CAUSES: Fabry's disease, Tangier's disease, familial amyloid polyneuropathy

TOXIC CAUSES: Chemotherapy, alcoholism, solvent exposure

AUTOIMMUNE CAUSES: Sjögren's syndrome, vasculitis/polyarteritis nodosa

AMYLOIDOSIS: Non-inherited forms of amyloidosis, e.g. lymphoma or plasma cell dyscrasias

INFECTIONS: HIV, hepatitis C, Lyme disease

IDIOPATHIC: For a relatively large percentage of cases, there is no identifiable cause of SFPN

❑**We discussed the potential treatments** that could include a dietary supplement containing **Alpha-Lipoic Acid** (600mg daily) and **Benfotiamine** (600mg daily). When clinically indicated, such products may be helpful to both diminish the symptoms of neuropathy, and to improve overall epidermal nerve health.
Additionally, investigators have shown benefit to using combination therapy that includes L-methylfolate, methylcobalamin (**B12**) and pyridoxal 5-phosphate (**B6**).

**References:** Ziegler D. Effect of 4year antioxidant treatment with alpha-lipoic acid in diabetic polyneuropathy: the NATHAN 1 trial. Diabetes 2007;56(Suppl.1):A2. Luong KV, et al.. The impact of thiamine treatmentin diabetes mellitus. J Clin Med Res 2012;4(3):153-160.

❑**This is an abnormal Sympathetic response which is consistent with a chronic pain syndrome. The progress of the treatment program is satisfactory.**

❑**Possibility of psychological pain, dependence and pain psychology follow up discussed**

❑ **The patient will follow up with the primary care physician for treatment and review of additional factors that can cause autonomic dysfunction. Fall precautions and patient medication list reviewed.**

❑ **Initiate treatment with compounding medication formulation (please see the prescription below).**

❑ Indications for genetic testing reviewed

Other-

_____
_____
_____
_____

**Sincerely,**

**_____**

**Leon Margolin M.D., Ph.D.**

**Patient Name: -------** **INS: Caresource** **DOB: -------** **Date: 07/07/2025**

**PLEASE INCLUDE PATIENT DEMOGRAPHICS/FACE SHEET AND PRESCRIPTION CARD**

PATIENT NAME_____ DOB:_____ SSN#_____
PHONE #_____ ADDRESS:_____
ALLERGIES:_____ DIAGNOSIS:_____

## MEDICATION ORDERS

- ❑ DIFLORASONE DIACETATE 0.05% Ointment (Sig: Apply 1-2g to affected area in a thin layer 1 to 3 times daily.)
- ❑ FLUTICASONE PROPIONATE 0.05% Cream (Sig: Apply up to 3g to affected area 2 times daily as directed. Avoid face, underarms and groin.)
- ❑ FLUOCINONIDE 0.1% Cream (Sig: Apply 1-2g to affected area in a thin layer 2 to 4 times daily. Use 14 days on 2 days off)
- ❑ CALCIPOTRIENE/BETAMETHASONE DIPROPIONATE 0.0005-0.064% Ointment (Sig: Apply 1-2g to affected area in a thin layer once daily. MaX of 8g/day and 100gm/week. Avoid face, underarms, and groin.)
- ❑ DESOXIMETASONE 0.05% Ointment (Sig: Apply up to 3g to affected area twice daily as directed max of 6g/day)
- ❑ CLOBETASOL PROPIONATE 0.05% Ointment (Sig: Apply up to 3g to affected area twice daily as directed. max of 6g/day)
- ❑ FLURANDRENOLIDE 0.05% Lotion (Sig: Apply to affected area 2 to 3 times daily)
- ❑ ALCLOMETASONE 0.05% Cream (Sig: Apply 1-2g to affected area 2 or 3 times daily)
- ❑ HALOBETASOL PROPIONATE 0.05% Ointment (Sig: Apply 2-3g to affected area twice daily. Max 50g per week)
- ❑ DOXEPIN 5% CREAM (Sig: Apply 1-2g to affected area 2-4 times daily)

## OTHER THERAPIES

- ❑ Naltrexone 1.5mg #90 capsules, or # _____ capsules
  Sig: _____ **Refill(s)** _____ **PRN** _____
- ❑ Naltrexone _____mg #90 capsules, or # _____ capsules
  Sig:_____ **Refill(s)** _____ **PRN** _____
- ❑ DICLOFENAC SODIUM 2% TOP SOLUTION 112GM
  (Sig: Apply 2 pumps to affected areas, Two times a day.)

## ADDITIONAL PODIATRY

- ❑ Fluconazole 1%; DMSO 50% Liquid (Sig: Apply to nail bed 2x Daily)
  QTY: 30ml
- ❑ Cimetidine 2%; DDG 0.2% Salicylic Acid 20% Cream (Sig: Apply to wart(s) 2x daily for 1 week. Then 1x daily for 3-6 weeks as directed or tolerated.)
  QTY: 30g
- ❑ Urea 40% cream (Sig: Apply up to 4 grams (4 pumps) to affected area 2 times daily as directed (up to 8 grams/day)) QTY: 180g
  CONJUCTION WITH Clobetasol 0.05% ointment
  (Sig: Apply up to 3 grams to affected area 2 times daily as directed (6 grams/day)) QTY: 180g

## TOPICAL THERAPIES

*may substitute bulk powder based on coverage determination or patient preference

- ❑ I. AMANTADINE 6% CYCLOBENZAPRINE 2% DICLOFENAC 3% PENTOXIFYLLINE 3% IBUPROFEN 1% AMITRIPTYLINE 2% + LIDOCAINE 5% Ointment*
  Sig: Apply 1-2g to affected area 2 to 4 times daily.
- ❑ II. DICLOFENAC 3% KETOPROFEN 5% IBUPROFEN 1% PENTOXIFYLLINE 3% + LIDOCAINE 5% Ointment*
  Sig: Apply 1-2g to affected area 2 to 4 times daily.
- ❑ III. DICLOFENAC 3% CYCLOBENZAPRINE 2% VERAPAMIL 3% PENTOXIFYLLINE 3% IBUPROFEN 1% + LIDOCAINE 5% Ointment*
  Sig: Apply 1-2g to affected area 2 to 4 times daily.
- ❑ IV. DICLOFENAC 3% TETRACAINE 7% + LIDOCAINE 5% Ointment*
  Sig: Apply 1-2g to affected area 2 to 4 times daily.

**To add controlled substances to the selected compound, please write on the line provided and include strength:**
_____

- ❑ V. LIDOCAINE 5% + ACYCLOVIR 5% Ointment*
  Sig: Apply sufficient quanity to cover the affected area up to every three hours, no more than six times per day, for 7 days maximum.
- ❑ VI. Other Requested Topical Therapy _____
  Sig:_____

**Comprehensive Pain Institute**
5245 E Main St.
Columbus, OH 43213
Phone: 614-557-6817
Fax: 614-453-8222

❑ LEON MARGOLIN - NPI: 1619178308

Please Check One:
❑ 240g ❑ 120g
Refills:_____
Day Supply: 30 days ____ Other

Signature: Substitution Permitted

Dispense as Written

Date Written

Comprehensive Pain Management Institute, LLC

**Informed Consent for Autonomic Study/PWV study**

Patient's Name _____ Date _____

I hereby authorize Dr. Leon Margolin or Associates or Assistants of his choice at Comprehensive Pain Management Institute, LLC to perform upon me/the patient named above the following EMG/NCV(s)

Nerve Conduction Study, Autonomic Study and/ or EMG testing

PLEASE INFORM THE DOCTOR

- IF YOU HAVE PACEMAKER OR DEEP BRAIN STIMULATOR
- IF YOU ARE OR COULD BE PREGNANT
- IF YOU HAVE TAKEN PLAVIX, COUMADIN, ANY OTHER BLOOD THINNER
- IF YOU HAVE AN AMPUTATED LIMB

Dr. Margolin has fully explained the nature and the purpose of this test and has also informed me of expected benefits and complications (from known and unknown causes), attendant discomforts and risks that may arise.

I have been given the opportunity to ask questions or request testing by an alternative provider, and all my questions have been answered fully and satisfactorily. All my questions about the charges for this test were answered. Dr. Margolin has fully explained to me that medical management including initiation or continuation of narcotic medications does not depend on my consent to this or any other procedure or test.

Patient's Signature: Date:

Physician's Signature Date:

Technician's Signature: Date:

Assumption of Risk and Complete Release and waiver of Liability

R-R interval testing, SSR (Sympathetic response), PWV, NCV & EMG Testing

Patient Name:_____ Date:_____

In consideration of permission to use today, and on all future dates, the property, facility, and services (Facilities); I, the undersigned patient, do hereby expressly agree:

1. That I was advised that abnormal test results of R-R interval (sympathetic response), NCV& EMG testing and other tests may be associated with the risk factors that can result in significant morbidity, disability and mortality (including but not limited to a sudden cardiac death).
2. That I was advised that Comprehensive Pain Management Institute, LLC is not responsible for monitoring compliance with the treatment plan or life style modifications related to these risk factors, I was advised that Comprehensive Pain Management Institute, LLC is not responsible for my appropriate follow up with the medical providers and my compliance with recommendations of other physicians related to these risk factors.
3. TO RELEASE ( Comprehensive Pain Management Institute, LLC ( CPMI) and all its successors, assigns , affiliates, administrators, employees and agents from, and AGREES NOT TO SUE ANY OR ALL OF THEM on account of or in connection with any claims, causes of actions, injuries , damages, cost or expenses related to these risk factors, morbidity, disability and mortality ( including but not limited to a sudden cardiac death) , whether or not caused by the negligence or other fault of (CPMI), or other equipment supplied by (CPMI).
4. THIS REALEASE shall be binding upon heirs, administrators, executors, assigns and legal representative.
5. TO WAIVE the protection afforded by any statue or law any jurisdiction whose purpose, substance and/ or effect is to provide that a general release shall not extend to claims, material or otherwise, which the person giving the release does not know to suspect to exist at the time of executing the release;
6. IF I IGNORE THIS AGREEMNT AND FILE SUIT, I WILL BE HELD RESPONSIBLE FOR ALL ATTORNEY FES AND COURT COST INCURRED BY (CPMI)
7. I HAVE READ AND UNDERSTAND THIS AGREEMENT, I UNDERSTAND THAT BY MAKING AND SGINING THIS AGREEMENT I SURRENDER VALUABLE RIGHTS, INCLUDING BUT NOT LIMITED TO, MY RIGHT TO SUE.

X_____ _____

(Signature) (Date)

**Patient Name: -------** **INS: Caresource** **DOB: -------** **Date: 07/07/2025**

Patient copy

**SSR / HRV (RR variability) Medical Necessity/Pre Test Questionnaire**

Atherosclerosis of the Aorta? **Yes / No**
***R09.89***

Beurger's Disease (inflammation or clotting in blood vessels In hands or feet)? **Yes/No**
***R09.89***

Peripheral Vascular Disease (PVD – Circulation disorders in blood vessels)? **Yes/No**
***R09.89***

Ateriovenous Fistula? **Yes/No**
***R09.89***

Raynaud's Syndrome (discoloration of fingers and/or toes when exposed to changes in temperature (cold or hot) or emotional events)? **Yes/No**
***R09.89***

Embolism of the upper limb/limbs (Artery obstruction in the arms)? **Yes/No**
***R09.89***

**SSR**: Type 1 Diabetes with neurological symptoms? **Yes/No**
***E10.40***

Do you ever have pain in your arms and/or legs? **Yes/No**
***G60.9***

Edema (swelling in arms and or legs? **Yes/No**
***G60.9***

Hypotension (very low blood pressure)? **Yes/No**
***I95.1***

Do you ever notice a tingling/numbness felling in your fingers, arms, legs or feet**?** **Yes/No**
***G60.9***

Reflex Dystrophy (Chronic Pain in limbs after injury, stroke or heart attack)? **Yes/No**
***G90.59***

Peripheral Neuropathy (a result of damage to your peripheral nerves, often causes weakness, numbness and pain, usually in your hands and feet. It can also affect other areas of your body)? **Yes/No**
***G90.09***

Do you smoke or have you ever smoked? **Yes/No**
***Z87.891***

Do you have hypertension? (High Blood Pressure) **Yes/No**
***I10***

Do you have history of CVA or TIA (Stroke or mini stroke)? **Yes/No**
***Z86.73***

Do you have a pain or insulin pump? **Yes/No**

**SSR:** Type 2 Diabetes with neurological symptoms? **Yes/No**
***E11.40***

Rapid Heart Rate (Tachycardia)? **Yes/No**
***R00.0***

Dizzy and or light headed when you stand up? **Yes/No**
***R55***

Idiopathic Peripheral Neuropathy? When the cause can't be determined, it's called idiopathic neuropathy. Includes numbness, tingling and pain in legs and or feet. **Yes/No**
***G60.9***

Do you experience Hyperhidrosis (Excessive sweating)? **Yes/No**
***R61***

Do you have Amyloidosis (abnormal deposits of protein in one or more organs or body systems)? **Yes/No**
***E85.8***

Reflex sympathetic Dystrophy (marked by burning pain, swelling, and motor and sensory disturbances especially of an extremity after an injury)? **Yes/No**
***G90.59***

Has anyone in your immediate family (blood relatives) been diagnosed with cardiovascular disease (CVD), or have had a heart attack? **Yes/No**
***Z82.49***

Has anyone in your immediate family (blood relatives) passed away from Sudden cardiac death Syndrome (SCD)? **Yes/No**
***Z82.41***

| | |
|---|---|
| Do you have history of CVA or TIA (Stroke or mini stroke)? **Yes/No** ***Z86.73*** | Do you have high cholesterol? **Yes/No** ***E78.5*** |
| Do you easily get cold hands and/or feet? **Yes/No** ***20.9*** | Do you often feel fatigued? **Yes/No** ***R53.83*** |
| Do you have a pacemaker or defibrillator? **Yes/No** | Are you pregnant? **Yes/No** |

X_____ _____

(Signature) (Date)

**SSR / HRV (RR variability) Medical Necessity/Pre Test Questionnaire**

| | |
|---|---|
| Atherosclerosis of the Aorta? **Yes / No** ***R09.89*** | Ateriovenous Fistula? **Yes/No** ***R09.89*** |
| Beurger's Disease (inflammation or clotting in blood vessels In hands or feet)? **Yes/No** ***R09.89*** | Raynaud's Syndrome (discoloration of fingers and/or toes when exposed to changes in temperature (cold or hot) or emotional events)? **Yes/No** ***R09.89*** |
| Peripheral Vascular Disease (PVD – Circulation disorders in blood vessels)? **Yes/No** ***R09.89*** | Embolism of the upper limb/limbs (Artery obstruction in the arms)? **Yes/No** ***R09.89*** |

**Patient Name: -------** **INS: Caresource** **DOB: -------** **Date: 07/07/2025**

**SSR**: Type 1 Diabetes with neurological symptoms?
**Yes/No**
***E10.40***

Do you ever have pain in your arms and/or legs?
**Yes/No**
***G60.9***

Edema (swelling in arms and or legs?
**Yes/No**
***G60.9***

Hypotension (very low blood pressure)?
**Yes/No**
***I95.1***

Do you ever notice a tingling/numbness felling in your fingers, arms, legs or feet**?** **Yes/No**
***G60.9***

Reflex Dystrophy (Chronic Pain in limbs after injury, stroke or heart attack)? **Yes/No**
***G90.59***

Peripheral Neuropathy (a result of damage to your peripheral nerves, often causes weakness, numbness and pain, usually in your hands and feet. It can also affect other areas of your body)?
**Yes/No**
***G90.09***

Do you smoke or have you ever smoked?
**Yes/No**
***Z87.891***

Do you have hypertension? (High Blood Pressure)
**Yes/No**
***I10***

Do you have history of CVA or TIA (Stroke or mini stroke)?
**Yes/No**
***Z86.73***

Do you have a pain or insulin pump?
**Yes/No**

**SSR:** Type 2 Diabetes with neurological symptoms?
**Yes/No**

***E11.40***

Rapid Heart Rate (Tachycardia)? **Yes/No**
***R00.0***

Dizzy and or light headed when you stand up?
**Yes/No**
***R55***

Idiopathic Peripheral Neuropathy? When the cause can't be determined, it's called idiopathic neuropathy. Includes numbness, tingling and pain in legs and or feet. **Yes/No**
***G60.9***

Do you experience Hyperhidrosis (Excessive sweating)?
**Yes/No**
***R61***

Do you have Amyloidosis (abnormal deposits of protein in one or more organs or body systems)? **Yes/No**
***E85.8***

Reflex sympathetic Dystrophy (marked by burning pain, swelling, and motor and sensory disturbances especially of an extremity after an injury)? **Yes/No**
***G90.59***

Has anyone in your immediate family (blood relatives) been diagnosed with cardiovascular disease (CVD), or have had a heart attack? **Yes/No**
***Z82.49***

Has anyone in your immediate family (blood relatives) passed away from Sudden cardiac death Syndrome (SCD)?
**Yes/No**
***Z82.41***

Do you have history of CVA or TIA (Stroke or mini stroke)?
**Yes/No**
***Z86.73***

Do you easily get cold hands and/or feet? **Yes/No**
***20.9***

Do you have a pacemaker or defibrillator? **Yes/No**

Do you have high cholesterol? **Yes/No** ***E78.5***

Do you often feel fatigued? **Yes/No** ***R53.83***

Are you pregnant? **Yes/No**

Staff/Billing copy