

The Importance of Parasympathetic Excess and Why “The Foot on the Brakes” is a Primary Dysautonomia

by

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ABSTRACT

Parasympathetic Excess PE is an abnormal parasympathetic response to a sympathetic challenge or stress. PE was first discovered and published circa 2010. It was dismissed by the leadership, mostly due to the current model of autonomic function which is the “see-saw” model. Unfortunately, the seesaw model only works for normal, healthy individuals, or the advanced chronically ill or aged patients. We have developed a model using the brakes and accelerator and other components of an automobile with an automatic transmission. This model retains the “see-saw” model. For normal individuals, normally the driver either has a foot on the brakes or on the accelerator; this is the “see-saw”. In cases of advanced illness or age, the “brakes are worn” and the driver either has a foot on the accelerator or not. A common abnormality, even while driving, is to drive with a foot on the brakes. This is protective, as in anxious drivers worried about what might happen to them. The Parasympathetics are considered protective of the body. PE is missed largely due to the fact that most of the overt Symptoms of PE are due to Sympathetic Excess (SE) – over acceleration. SE may lead to heart disease, heart attack and stroke, but SE is also compensatory for PE (like over-acceleration is compensating for the foot being on the brakes). In fact, if only the SE (Tachycardia, Hypertension, excess or prolonged inflammation or histaminergic responses, pain, anxiety, and Hyperglycemia) is treated, often patients feel worse or do not seem to respond, and in the long run, treating SE only when it is a symptom (compensating for PE) the mortality risks of SE are more likely to be realized, because the body works to compensate for PE and now for the treatment to reduce SE, because PE still needs to be overcome, and the brakes are worn out faster; thereby unable to slow the car and a crash occurs – that is the heart attack or stroke. Treating PE removes the foot from the brakes and thereby, organically, normalizes SE and restores proper P&S balance. Here we discuss the importance of PE, its symptoms, treatments and therapies, and outcomes, based on a 10,000-patient database from four suburban practices.

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INTRODUCTION

Parasympathetic Excess (PE) is an abnormal Parasympathetic response to a Sympathetic challenge or stress. PE was first discovered and published 2010 [1]. It was dismissed by the leadership, mostly due to the current

model of autonomic function which is the “see-saw” model. Unfortunately, the seesaw model only works for normal, healthy individuals, or advanced chronically ill or aged patients. We have developed a model using the brakes and accelerator and other

components of an automobile with an automatic transmission. This model retains the “see-saw” model. For normal individuals, normally the driver either has a foot on the brakes or on the accelerator; this is the “see-saw”. In cases of advanced illness or age, the “brakes are worn” and the driver either has a foot on the accelerator or not. A common abnormality, even while driving, is to drive with a foot on the brakes. This is protective, as in anxious drivers worried about what might happen to them. In this way, the Parasympathetics are considered protective, in addition to promoting rest and digestion. As determined by Singer, a little more Parasympathetic activity is cardio-protective [2], and protective of all systems [3]. PE is missed largely due to the fact that most of the overt symptoms of PE are due to Sympathetic Excess (SE) – over acceleration (a beta-Adrenergic response, β SE). β SE as a primary dysfunction may lead to heart disease, heart attack and stroke. This is not contested. However, β SE is also compensatory for PE (over-acceleration is compensating for the foot being on the brakes). In this sense it is secondary β SE is secondary to PE. In fact, if only the β SE (Tachycardia, Hypertension, excess or prolonged inflammation or histaminergic responses, pain, anxiety, and Hyperglycemia) is treated, treated as a primary disorder, often patients feel worse or do not seem to respond. In the long run, treating β SE as the primary (only treating symptoms) when it is secondary to PE (compensating for PE), increased the mortality risks of β SE. These reason increased risks are more likely to be realized in these cases, is because β SE is already working to compensate for PE and now with treatment to suppress β SE, the body must

find ways to defeat the treatment of β SE as well, because PE still needs to be overcome. In the model, this serves to wear the brakes faster; thereby, the brakes will not be able to slow the car and a crash occurs. The crash is the heart attack or stroke. Treating PE, removes the foot from the brakes and thereby, organically, normalizes β SE and restores proper P&S balance.

P&S Monitoring provides more information than all other types of autonomic testing [3]. One such piece of more information is independent, simultaneous measures of Parasympathetic activity [1]. The current thought is that there is- no known upper limit to Parasympathetic activity. However, there must be given Bradycardia, Hypotension, Depression-like symptoms, and so-called Vagal Episodes, including fainting. Current methods of autonomic monitoring, including waveform assessment, recognize that the better the response curve in the cardiogram appears (*e.g.*, Respiratory Sinus Arrhythmia) the more Parasympathetic activity that is generating it, therefore the healthier the patient. A “perfect curve” must mean optimal health. This is not always the case. P&S Monitoring quantifies these responses and thereby provides more information, including a range for excessive Parasympathetic activity, *aka.*, PE.

METHODS

A database of 8128 consecutive, serial patients (57.3% Female; average age of 56.5 years; age range: 12 to 100 years) were followed for up to a six-year period, in four large suburban practices (two cardiology practices in the Philadelphia, PA and Memphis, TN areas, one Neurology practice in the New York City area, and one Internal

Medicine practice in the Minneapolis, MN area) drawing from both urban and suburban populations. P&S function was assessed noninvasively using the Physio PS, Inc. (Atlanta, GA) software (ANX 4.0 P&S Monitor). The ANX 4.0 computes simultaneous, independent measures of P&S activity based on continuous, time-frequency analysis of Heart Rate Variability (HRV) with concurrent, continuous, time-frequency analysis of Respiratory Activity (RA) [3].

P&S Monitoring

HR Variability (HRV) analyses alone are mixed measures of P&S activity. Because HRV terms are based on a measure of cardiac function alone, and the heart is controlled by both autonomic (P&S) branches. HR and BP terms are mixed measures of both P&S activity. As a result, HRV terms are mixed measures of both P&S activity and require assumption and approximation to specify P&S activity.

To eliminate the need for assumption and approximation, a second mathematically independent signal is required (*i.e.*, a signal from a totally different measurement involving the autonomic nervous system).

As demonstrated and validated by Akselrod's group at MIT/Harvard [4,5, 6,7], the second independent P&S measure is Respiratory Activity (RA). This satisfies the algebraic requirement for a system with two independent components, fully characterizing the system, eliminating the need for assumption and approximation when, in this case, differentiating Parasympathetic from Sympathetic activity. P&S Monitoring combines spectral analysis of HRV and spectral analysis of RA to measure P&S activity. [3]

The clinical study employed to determine P&S activity includes four well-known autonomic challenges [8,9,10], separated by resting baseline periods. These six periods are labeled in the figures as: A) Resting Baseline¹¹, B) Deep Breathing, C) Valsalva baseline, D) Valsalva maneuvers, E) Stand baseline, and F) Stand (postural change). The Stand challenge is a postural change challenge, which is equivalent tilt-testing [12]. The Stand challenge is a physiologic activity and therefore inherently safer and

more comfortable for the patient, arguably leading to more reliable results [13]. The Stand challenge enables autonomic testing to be performed in smaller clinics, and in shorter time periods. From a safety point of view, the independent measures of P&S activity obviate the need for overt symptoms to be demonstrated, thereby inherently improving the safety of the study.

P&S Monitoring also facilitates reading P&S responses in the presence of arrhythmia [14]. Given that POTS patients may present with palpitations and possible arrhythmia (typically benign, *e.g.*, sinus arrhythmia), arrhythmia patients were included in this analysis.

Therapy Options

There were three therapy options offered to patients: Pharmaceutical [3], non-Pharmaceutical [15], or a combination of the two. Many patients present after many years of many other physicians and providers diagnosing symptoms and prescribing more and many medications. More is not better in P&S treatment, for it typically leads to more side-effects, interactions, and symptoms and therefore more P&S dysfunction. For example, antidepressants may include anti-cholinergic effects, but only at the lowest doses, and since many antidepressants are not offered at low enough doses, the options are limited. When used off-label, at the lowest possible doses only, they may then be helpful without causing additional depression-like symptoms. The low-dose pharmaceutical options are homeostatic doses and have been found to be interchangeable with the supplement and lifestyle modifications also recommended [14]. A major difficulty in treatment is the sensitivities that patients have developed,

not necessarily to the pharmaceutical agents themselves, but to the fillers and capsules/coatings used to convey the agent. This is another reason for providing non-pharmaceutical options.

Pharmaceutical Therapy Options

Pharmaceutical therapy options were prescribed based on patient history [3,16]. In general, the primary treatment for PE is Nortriptyline 10.0 mg, qd, 12 hrs before waking. The secondary treatments are Amitriptyline 10.0 mg, qd, 12 hrs before waking or Duloxetine, 20mg, qd, dinner. If Sympathetic Excess (SE) or Tachycardia or high BP was demonstrated low dose Sympatholytics are prescribed to protect accordingly.

Non-Pharmaceutical Therapy Options

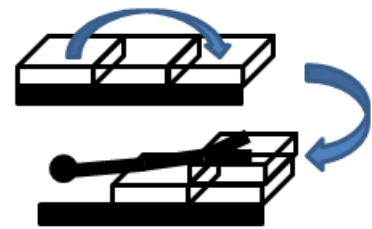
In general, psychosocial stress reduction was recommended with history-specific antioxidant and supplement recommendations to reduce oxidative stress and improve blood flow. Non-Pharmaceutical therapy options were offered if patients were intolerant or unresponsive to the pharmaceutical options. In general, (1) Alpha-Lipoic Acid, 600 mg tid, titrated as needed and tolerated, and (2) proper daily hydration with electrolytes were recommended. For PE, a low-and-slow exercise regimen was recommended for six months. The maximum exercise in low-and-slow is walking at no more than two miles per hour for 40 contiguous minutes per day [14]. Often this was augmented, early in the therapy especially if the patient reported significant sleep difficulties, by no more than 20 minutes of supine, up to 15° head-down posture (*e.g.*, by rearranging couch cushions, see insert, right) around two hours

before bed-time and up to three times per day, as needed to relieve brain-fog, anxiety, tension headache, etc.. Autonomically induced arrhythmia (Sinus Arrhythmia) was treated based on underlying etiology (*e.g.*, PE or SE).

This is an observational study. Patient testing and clinical outcomes measures were collected as an

authorized part of the subjects' care and treatment given their clinical history. All data were handled according to HIPPA regulations. Data were analyzed, statistically, with SPSS v 22.0.

15° Head-Down Posture



RESULTS

P&S Tests were administered to 8,128 patients over six years. Of these 8,128 patients, 170 presented with Arrhythmia throughout the whole test (*e.g.*, Atrial Fibrillation) and were omitted from this analysis, leaving 7,958 total patients that were administered 13,070 tests over six years in four clinics (Table 1). At rest, on average, these patients presented with normal HR (73.6 bpm), elevated systolic BP (129.4 mmHg), and normal diastolic BP (72.4 mmHg). At baseline testing they're autonomic activity levels were within normal range (the average Sympathetic measure, LFa = 2.3 bpm², and the average Parasympathetic measure, RFa = 2.0 bpm²; (Normal resting P&S activity: 1.0 < LFa, RFa < 10.0 [3]), and their resting balance (SB) was in the high normal range (normal SB: 0.4 < SB < 3.0 [3]).

Table 1: P&S Test Data. Demographics and Resting Baseline and Valsalva results of the cohort by test. Of the 8128 patients followed, 170 presented with Arrhythmia throughout the whole test (*e.g.*, Atrial Fibrillation) and were omitted from this analysis, leaving 7958 total patients that were administered 13070 tests over six years in four clinics.

Test #	Demographics			Resting Baseline						Valsalva	
	N	Age (yrs)	BMI (lb/in ²)	HR (bpm)	sBP (mmHg)	dBP (mmHg)	LFa (bpm ²)	RFa (bpm ²)	SB	RFa (bpm ²)	ΔRFa (bpm ²)
Tot	13070	56.5	28.68	73.6	129.4	72.4	2.3	2.0	1.8	10.1	4.08
1	7958	53.1	29.04	74.7	128.7	73.3	2.6	2.3	1.8	11.0	4.68
2	2226	57.2	28.3	72.7	128.8	72.0	2.3	1.9	1.9	9.4	4.23
3	1074	61.3	28.32	71.9	129.8	71.0	1.8	1.6	1.9	11.0	2.96
4	617	64.6	28.52	70.6	130.8	69.6	1.7	1.3	1.9	6.69	1.89
5	400	67.4	27.03	70.3	132.3	69.4	1.5	1.2	2.0	8.32	1.12
6	255	68.1	28.37	70.8	133.9	69.9	1.5	1.5	1.9	5.6	1.85

Δ, Delta (indicating the change in the associated parameter from resting baseline); #, Number; BMI, Body Mass Index; HR, Heart Rate; dBP, Diastolic Blood Pressure; LFa, Low Frequency area (the measure of Sympathetic activity); N, Number; RFa, Respiratory Frequency area (the measure of Parasympathetic activity); SB, Sympathovagal Balance (=resting LFa/Resting RFa, an average of ratios, not a ratio of the averages, unitless); sBP, Systolic Blood Pressure; Tot, Total;

Table 2: P&S Test Data. Stand results of the cohort presented in Table 1.

Test #	Stand									
	LFa (bpm ²)	RFa (bpm ²)	HR (bpm)	sBP (mmHg)	dBP (mmHg)	ΔHR (bpm)	ΔLFa (bpm ²)	ΔRFa (bpm ²)	ΔSYS (mmHg)	ΔDIAS (mmHg)
Tot	11.4	5.6	81.9	131.0	76.2	8.3	3.0	-0.2	1.6	3.9
1	11.3	5.7	83.4	130.7	77.2	8.7	3.9	-0.4	1.9	3.9
2	10.4	6.1	81.0	130.2	76.0	8.3	1.1	1.3	1.5	4.1
3	16.1	6.3	79.6	131.0	74.9	7.6	1.3	-1.5	1.5	4.0
4	9.4	4.1	78.0	132.0	74.0	7.4	3.4	-0.1	1.2	4.6
5	16.2	4.6	77.6	132.8	72.8	7.3	-1.7	-2.6	0.6	3.6

6	3.3	3.2	77.9	133.9	73.5	7.1	-2.7	-0.5	0.0	3.6
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Δ, Change in a parameter from resting Baseline. See Table 1 for other abbreviations.

The Deep Breathing results were within normal range (data not shown). The Valsalva Parasympathetic results (Table 1) are also within normal limits (the absolute value is age adjusted and the expected change is less than a 400% increase, including decreases) [3]. Averaged out of these result are the individual instances of Parasympathetic Excess (PE) during the Valsalva challenge. The Valsalva challenge simulates stress responses, both healthy and unhealthy. Valsalva PE contributes to the Vasovagal Syncope (VVS) findings if Stand SE also presents (see Discussion).

The Stand challenge results are presented in Table 2. The P&S responses to Stand are baseline adjusted. Normally, on average, the Parasympathetics first decline to minimize the Sympathetic response, then the Sympathetics increase [3]. Normally, over the five minutes of the Stand challenge, the dominant net Sympathetic response is an alpha-Sympathetic (alpha-Adrenergic) response. The net, average, beta-Sympathetic (beta-Adrenergic) response is normally near zero. Any increase in average Parasympathetic activity over the five-minute Stand challenge, or any decrease in alpha-Sympathetic activity, is abnormal. Normally, the average HR and BP responses to the Stand challenge are 10% increases in each measurement.

On average (Table 2), the change in Parasympathetic activity (ΔR_{Fa}) is a 0.2 bpm² decrease and the change in Sympathetic activity (ΔL_{Fa}) is a 3.0 bpm² increase. These are normal. The HR

increases well into the normal range ($\Delta HR = 8.3$ bpm), but not excessively. The BP increases are weak ($\Delta BP = 1.6/3.9$ mmHg), indicating that on average the typical patient presented with a level of Orthostatic dysfunction, typically, Orthostatic Intolerance.

DISCUSSION

Overall, these patients would appear normal to the average physician working to maintain them. This is due to the fact that most of these patients were assessed by the other physicians at rest (sitting or supine), and they've had many doctors over many years working to maintain them in a normal resting state. (The typical patient presents after seeing at least a dozen physicians over a decade with at least one referral to Psychiatry.).

However, the autonomic nervous system is rarely at rest. This is the reason for the needed challenges, to further probe the function of the P&S branches. The true power of P&S and autonomic testing is in determining the individual patient's individual responses to rest and challenges.

Averaging P&S responses over a large population loses the individuality of the patients' responses. As we will see (Table 2), the typical problem (especially in younger patients) occurs in response to the Stand, or postural change, challenge. This challenge serves several main purposes: 1) it helps to document the causes of

lightheadedness due to an autonomic dysfunction; thereby 2) differentiating Orthostatic dysfunction from Syncope (see below); 3) differentiating causes of lightheadedness from dizziness (a Vestibular dysfunction) and, 4) it also serves to test the coordination between the P&S branches. The last purpose may be the more important purpose from an autonomic perspective.

Oftentimes, when there are Stand challenge abnormalities (Table 2), resting BP or resting SB will be elevated or high. We have found these elevated or high results to be a compensatory mechanism to help maintain proper cerebral perfusion and prevent lightheadedness and other symptoms associated with poor cerebral perfusion, including Cranial Nerve dysfunction (if the brain is poorly perfused so are the cranial nerves and the retina).

The fact that on average patients demonstrate Orthostatic dysfunction upon standing suggests a closer look into the stand responses. While the average Parasympathetic response to Stand challenge is an appropriate decrease of activity, and while there is no known grading of the measure (either the individual patient has PE or not), the fact that the magnitude of the average response is small (only 0.2 bpm², Table 2) indicates that there are many that do show an increase in Parasympathetic activity with Stand (PE) which is abnormal. PE underlies possible (pre-clinical) Vasovagal Syncope (“Vagal” is a synonym for Parasympathetic). Similarly, while the average (alpha) Sympathetic response to the Stand Challenge is an appropriate increase of activity, and while there is no known grading of the measure (either the individual patient has α -Sympathetic Withdrawal, α SW, or not), the fact that the magnitude of

the average response is small (3.0 bpm², Table 2) indicates that there are many that do show a decrease in α SW which is abnormal. α SW underlies possible Orthostatic dysfunction. The prevalence of possible Orthostatic dysfunction is further indicated by the weak BP responses to the Stand challenge.

PARASYMPATHETIC EXCESS – THE DEFINITION AND SYMPTOMS

Parasympathetic Excess (PE) is an abnormal Parasympathetic response to a Sympathetic challenge (*e.g.*, from the clinical exam: Valsalva or Stand) or an abnormally low Ratio of S-to-P (known as Sympathovagal Balance or SB = resting S/P) [3] (see Figure 1). PE combined with Stand challenge beta-Sympathetic Excess (β SE, a beta-adrenergic response), whether documented as an instantaneous response as seen in the Trends plot (see Figure 2) or an average response as seen in the Stand response plot (see Figure 3), defines (pre-clinical) Vasovagal Syncope (VVS).

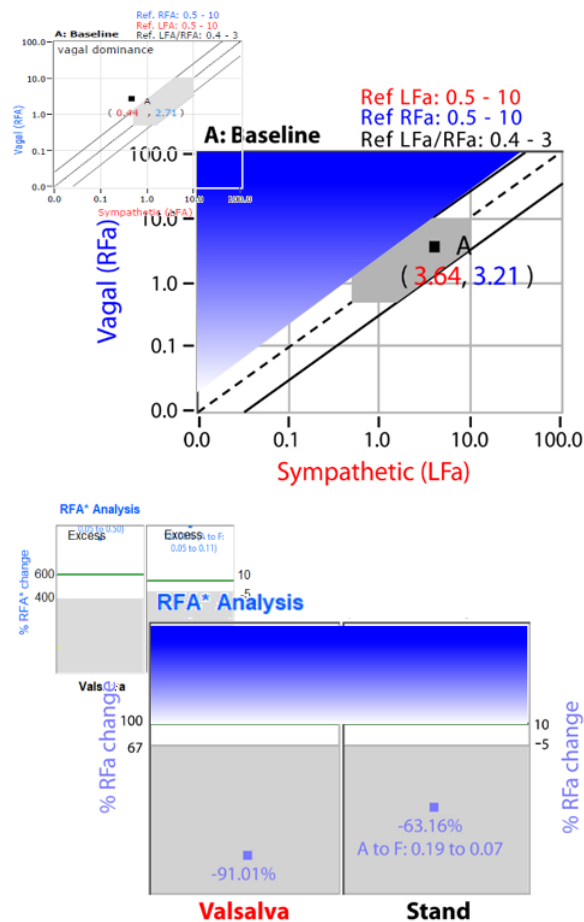


Figure 1: Indications of Parasympathetic Excess (PE) from the P&S clinical study as found in different clinical challenges. Top plot depicts the excessive Parasympathetic range for Resting Baseline. The bottom plot depicts the excessive Parasympathetic ranges for Valsalva (left panel) and Stand (right panel)/ The small, insert graphs provide an example of an abnormal response [3,17]

Note: an α SW response is possible only with the Stand challenge. SW is the P&S definition of Orthostatic dysfunction. Also, Stand PE or Stand β SE, either instantaneous or on average, see above, may mask α SW,

it may still be inferred by abnormal Stand BP response (Orthostatic Intolerance or Orthostatic Hypotension depending on the severity of the BP drop upon standing) or abnormal Stand HR response (POTS or pre-POTS responses). In this way VVS may be differentiated from all forms of Orthostatic dysfunction. This, thereby enables both the PE for VVS and SW for Orthostatic dysfunction to be treated and in most cases relieved. Without P&S Monitoring, it is not possible to differentiate POTS from VVS, even though it is well known to be comorbid in at least $\frac{1}{3}$ of all POTS patients. Within

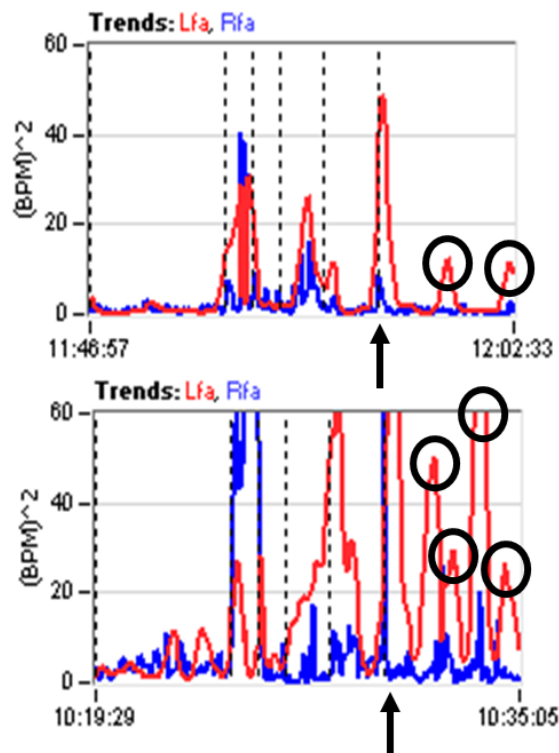


Figure 2: Examples of (pre-clinical) Syncope spikes as documented by the circled red peaks found during the latter, quiet stand portion of the Stand challenge. The arrows indicate the expected Sympathetic surge that occurs during the active part of standing-up, known as the Gravitational Response. [3,16]

this cohort, 3735 patients demonstrated POTS (1015) or pre-clinical POTS (2720) and 1878 patients demonstrated VVS; a comorbidity ratio of 50.3%.

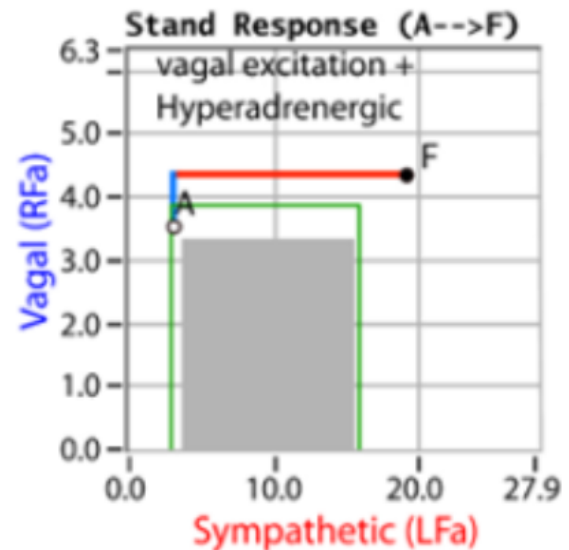


Figure 3: The presentation of PE with Stand Challenge SE, a definition of Vasovagal Syncope. [3,16]

α SW, indicating Orthostatic dysfunction, may be masked by PE or β SE. One clue to this comorbidity is that patients do not faint from the Orthostatic dysfunction, Postural Orthostatic Tachycardia Syndrome (POTS). The tachycardia prevents it. Those with POTS that do faint, also have VVS. P&S Monitoring detects both, especially in the pre-clinical phase. This enables both to be treated simultaneously, helping to prevent fainting and its co-morbidities, including falling.

The Parasympathetics influence vasodilation and the efficacy of the heart in pumping blood to the brain; thereby, affecting

cerebral perfusion. They also uniquely control and coordinate Immune function, GI motility, and Hormone systems. This is the basis for the symptoms of PE as a result of poor cerebral perfusion, including: 1) fatigue, 2) the tendency to feel faint, 3) lightheadedness, 4) exercise intolerance, 5) sleep disturbance, 6) memory and cognitive dysfunction, 7) “brain fog”, 8) frequent headache or migraine, 9) unexplained arrhythmia (palpitations with anxiety like symptoms), 10) shortness of breath, 11) unexplained seizure activity (Myoclonus), 12) Cranial Nerve dysfunction (abnormal vision, auditory, vestibular, olfactory, taste, and facial sensations), and 13) symptoms of Anxiety, Depression, Anxiety/Depression disorders (*e.g.*, Bipolar Disease), Attention disorders (*e.g.*, ADD/ADHD), Obsessive disorders (*e.g.*, OCD), and other psychological disorders may be mimicked by poor cerebral perfusion.

PE may also lead to upper and lower gastrointestinal motility abnormalities, urinary dysfunction, both incontinence and urgency. PE may be associated with hormone dysregulation. First check Thyroid levels, then reproductive hormone levels. We also find that supplemental growth hormones in adults adversely affect the P&S systems as well. PE is associated with auto-immune-like symptoms, or difficult to control BP, blood sugar, or weight.

Depression-like symptoms and symptoms of sleep disorders are due to the hypoperfusion of the brain where the brain is underactive. The rest of the psychological-like disorders are due to “adrenaline-storms” and other neurological forms of cerebral hyperactivity that are meant to increase cerebral perfusion, such as ADD/ADHD, OCD and perhaps high functioning Autism. These may also be

ways of attempting to compensate for poor cerebral perfusion.

Damaged nerve responses are typically types of hyperactivity before nerve healing or death. With P&S and end-organ testing, typically one must reassure the patient of healthy organs, and that it is the P&S nerves that are malfunctioning causing the organs to act as if they are dysfunctional. Then plan effective P&S treatment with properly set expectations. Setting expectations is most important in addressing and embarking on a therapeutic algorithm individualized to the specific patient’s own physiologic needs. P&S treatment is not a “10-day” relief program. Think of it more as a process of breaking a bad habit and developing and establishing a good habit. It often takes months.

SUMMARY

The “break and accelerator” model for the P&S nervous systems, respectively, improves on the “see-saw” model commonly taught. The improvement helps to differentiate primary causes of β SE from secondary causes. While treating primary β SE is important and may be lifesaving, treating secondary β SE as primary can accelerate the onset of the mortality risks associated with β SE. Secondary β SE is differentiated from primary β SE by PE or α SW.

The main reason why treatment of secondary β SE accelerates associated mortality risks, is because secondary β SE is typically compensatory for the effects of PE or α SW. PE and α SW may underlie Vasovagal Syncope and Orthostatic dysfunction, respectively, causing poor cerebral and perhaps coronary perfusion, as well as perfusion of all structures above the

heart. Treatment that attempts to limit β SE and the body's attempt to properly perfuse, forces different (perhaps less efficient) compensatory functions to be utilized or forces the body to defeat the therapy. In other words, not only do the β Sympathetic mechanisms have to compensate for the primary causes of poor perfusion, PE or α SW, but with β SE treatment the body also has to compensate for the medication attempting to limit the primary compensatory function(s). Often times, patients either do not respond properly or do not comply because they end up feeling worse.

Often times recognizing β SE as a compensatory function is difficult because patients are typically only assessed while resting (either seated or supine). When PE and SW are abnormal responses to postural change (standing or sitting up) these abnormalities are missed, and only the β SE is documented. It is important for patients to understand this point as they have often seen a number of physicians prior to learning this and have lost confidence in the health care system. Understanding that it is common to miss PE or α SW because it's not tested for, helps to restore confidence. It is then easier to help the patient understand how the poor cerebral perfusion caused by PE or SW may also lead to a number of other disorders that may be difficult to manage as well, including: Depression/Anxiety and related syndromes, ADD/ADHD, OCD not helped with psych meds and in some cases high functioning Autism; Hypertension not helped with antihypertensives, inflammatory auto-immunity with no known autoantibodies; Womens' health issues, Mast Cell Activation Syndrome, and Chronic

REFERENCES

Fatigue Syndrome. These are symptoms of P&S dysfunction. In many cases Anxiety, ADD/ADHD, OCD, and in some cases high functioning Autism, may be themselves compensatory mechanisms of an over-active brain attempting to compensate for poor perfusion on a more persistent basis. In all of these cases, it is true that there is over-acceleration (β SE), however, it may be true that a foot is on the brakes as well, forcing the over-acceleration just to reach normal speed and feel normal in life.

PE is "driving with the foot on the brakes" and may lead to depression, hypotension, and bradycardia, as examples. PE with β SE is the additional information that defines Vasovagal Syncope. α SW is "not enough gas getting out of the tank to the engine" and leads to blood pooling in the lower extremities also causing poor circulation to the periphery, as associated with Orthostatic dysfunction, as well as effecting coronary and cerebral perfusion. β SE, leading to high, resting BP or HR, may also be the over-acceleration needed to "get more gas out of the tank to the engine." With β SE and the additional information of PE and α SW, POTS and VVS may be differentiated and treated simultaneously if comorbid. (POTS: SW underlies the 'O' in POTS and β SE underlies the 'T' in POTS; VVS: PE is the Vagal component and β SE underlies the Syncope component.) A common result of PE is that patients are difficult to manage, such as difficult to managed BP, blood sugar, hormones, weight etc. The additional information from P&S monitoring helps to improve patient outcomes, restoring quality of life and productivity.

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