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Review Article

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Why only Manage Anxiety?!? Anxiety may be Cured!! A Review

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Background

Anxiety is indeed a real mental dysfunction [1]. However, there are many who are diagnosed with Anxiety, but may only have Anxiety-like symptoms. A significant clue to Anxiety-like symptoms is if a patient has been prescribed medicine, like Anxiolytics, for Anxiety for six months or more, and s/he still has significant bouts of Anxiety. The Anxiety has only been managed and not relieved or cured. There may have more than Anxiety to consider, or there may not have been Anxiety at all; only symptoms. A similar argument may be made of Depression-Anxiety syndromes, like Bipolar Disease and Manic-Depression disorders, as well as ADD/ADHD other attention and hyperactivity disorders, including OCD and perhaps high functioning Autism. There are conditions that cause poor blood flow to the brain and thereby poor brain or cerebral perfusion that may cause the very symptoms listed above. It may not be an actual mental defect, but an Autonomic or Cardiovascular deficit. For example, the Parasympathetic and Sympathetic (P&S) branches of the Autonomic Nervous System control and coordinate the cardiovascular system (as well as every other system and organ of the body). If the P&S nervous systems are in abnormal states (as discussed below) that prevent proper brain perfusion, one or both of two responses may occur. One response is that the brain responds to the poor perfusion by causing the release of adrenaline (known as an "Adrenaline Storm") to call for more blood. The Adrenaline Storm itself may cycle Anxiety-like symptoms for as long as the Adrenaline Storm lasts. This condition is accentuated and even promoted by a background state of sub-clinical depression where the sub-clinical depression is a result of marginal or poor brain perfusion (the brain is partially "asleep" which mimics depression). These states often involve all of the familiar accompanying symptoms, including: fatigue, exercise intolerance, sex dysfunction, sleep or GI disturbance, lightheadedness, persistent weight gain, cognitive dysfunction or "brain fog", and frequent headache or migraine.

The other response is activity or even hyperactivity where the patient "loves" to exercise or be active (mentally or physically) as much as possible, because the skeletal muscles help to move blood around the body, helping the heart to pump blood to the brain, thereby relieving the brain of the "worry" of not receiving enough blood. In cases of mental hyperactivity, the brain's requirement for the majority of the body's resources is also a means of helping the heart pump more blood to the brain (remember those difficult and long exams?). This activity can range from an inability to sit or stand still to the need to run 10 miles a day to frequent waking throughout the night and apparent insomnia.

The main reason why the abnormal P&S states are not well known is that with current Autonomic testing, only the *total* Autonomic state is measured. In most people with Anxiety or any of the other disorders mentioned, the total Autonomic state or function appears normal in those tests. For example, consider the following:

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Pato M, et al., Cardiol Cardiovasc Med 2024
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1. Since total Autonomic function (T) is the sum of Parasympathetic (P) function and Sympathetic (S) function (T = P + S);
2. As taught in medical school with the "see-saw" model, balance is the key to normal Autonomic function, and
3. Assume, in this example, normal for T for the individual patient is 4, then

The implicit assumption is that P = 2 and S = 2 (P+S = 2+2 = 4 = T); a balanced way to add to 4. Therefore, the patient is normal, physiologically. If all other physiological tests are within normal limits, the patient is then often referred to psych-eval.

However, if P = 1 and S = 3, T is still 4, but P&S are in abnormal states. Typical ANS testing still measures a 4. Even though this is an abnormal autonomic state, the total is '4' and the patient is typically normal at rest, because it is the main function of the P&S nervous systems to maintain normal function even when they themselves are in an abnormal state. Furthermore, since most providers only test patients at rest, they better be normal because they have many working very hard to keep them normal … at rest! (see resting baseline plots below). Only P&S testing, based on Cardio-Respiratory testing [2], differentiates P from S and may determine if P&S are 2&2 or 1&3 or in any other state. If we think of the P&S nervous systems like the brakes and accelerator of your car, the "see-saw" model is included under normal conditions: either your foot is on the brakes or your foot is on the accelerator; like a "see-saw" only one side is up at any one time. However, this only explains the resting, normal state. Otherwise, the "see-saw" model fails. The brake and accelerator model provides a better explanation. In the above abnormal state (P&S = 1&3), this is like driving a car with a foot on the brakes. The car still goes, but much more gas is required (read that as adrenaline) to over-accelerate and over-stress the engine (read that as use much more Sympathetic activity), just to get to normal speeds. This also excessively wears on the brakes and, in the long-run, accelerates the progression of autonomic dysfunction. If the patient does not "over-accelerate and over-rev the engine," then they do not reach normal speeds and they feel sluggish and fatigued, depressed or brain-fogged, because not enough "gas" (read that as blood) gets to the "engine", the brain in this example. This may simulate depression when resting or are in low energy states. So, they fall behind and then have to "step harder on the gas."

"Stepping on the gas" is like the Adrenaline Storm or ADD/ADHD or OCD. This causes the Anxiety-like symptoms, until the patient catches up to the rest of the "traffic." Then they ease off to also help reduce the stress, and then they begin to fall behind again; and the cycle continues. Either or both of two autonomic dysfunctions may cause this: 1) one is known as Parasympathetic Excess (PE [3], your foot is on the brakes) [2], and 2) the other is known as Sympathetic Withdrawal (SW [4], an alpha-Sympathetic response, even if you release the brakes, either you do not hit the accelerator enough; or you do, but sufficient fuel is not getting to the engine from the gas tank) [2]. The Adrenaline Storm or the attention abnormalities, referred to above, as well as many of the symptoms of Anxiety are beta-Sympathetic responses. (Remember, there are at least two parts of the Sympathetic nervous system.) Anxiolytics may only exacerbate the condition by limiting how much the patient is able to over-accelerate while trying to catch up. However unlike a car, the body has several pathways to increase blood flow to the brain, and medicine (like Anxiolytics and similar mediations to slow things down) is only able to block a few of them. So, the body seems able to defeat the therapy (because in reality things are already too slow, remember the patient is riding the brakes, not only over-accelerating), even though high doses may be prescribed. As a result, the patient may be accused of not complying with the therapy when they know they are.

SW often includes a condition known clinically as Orthostatic dysfunction [4], which includes POTS and Orthostatic Hypotension (OH) [2]. Here the blood pools in the feet and ankles. The (alpha-)Sympathetics do not sufficiently vasoconstrict and thereby do not help move the blood up to the abdomen, thereby making it difficult for the heart to pump the blood to the brain, leading to poor cerebral perfusion. The same conditions and same symptoms result, leading to the Adrenaline Storms and then to Anxiety with possible depression. (The depression is from persistent poor cerebral perfusion.) The cyclic nature of the Adrenaline Storms and symptoms of these conditions explain the manic-depression and bipolar syndromes as well as the fact that the Anxiety is not persistent 100% of the time. In cases of attention disorders, the inability to attend and the reason for hyperactivity is because other systems of the body are being recruited to help the heart pump blood to the brain. Brain stimulants, like Adderall and Ritalin, help temporarily by chemically stimulating the brain and resembling a longer Adrenalin Storm. Similarly, caffeine and other such stimulants have similar effects, enabling patients to self-medicate. In fact, many of these sorts of patients have found that they become exercise fanatics, and the harder the exercise the better they feel … while exercising. This is because the muscles involved in the exercise are helping to pump blood to the brain. They are more alert and awake, of course they love it … until …. After the exercise, they often "crash." Without the help of other systems or the muscles, their hearts are not strong enough (or more to the point the P&S nervous systems are not permitting the heart to be strong enough) to do the post-exercise or post exertion (in the case of mental activities, like hard exams in school) work needed to recover from the exercise or exertion. This is another clue that the Anxiety may also involve the P&S nervous systems.

Pato M, et al., Cardiol Cardiovasc Med 2024
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Without the ability to differentiate P from S without assumption and approximation, P&S activity cannot be measured effectively to diagnose the physiologic causes of Anxiety-like symptoms. With PE & SW, we have already mentioned a couple of the Dysautonomias or Autonomic Dysfunctions that may cause Anxiety-like symptoms. Others may include Orthostatic Intolerance (OI, another SW disorder [4], like POTS and OH), Vasovagal Syncope (VVS, a PE disorder [3]), other forms of Syncope (Neurogenic and Cardiogenic Syncope or combinations of the two) which may also be the results of over-acceleration (beta-Sympatehtic Excess, or SE [2]), and certain types of Arrhythmias which may or may not involve autonomic dysfunction causing inefficient pumping of blood to the brain [5]. For example, many patients with Anxiety-like symptoms have POTS (αSW causing the Orthostatic – the 'O' in POTS – with Tachycardia – the 'T' in POTS a βSE response compensating for the 'O'), co-morbid with Vasovagal Syncope (VVS, PE – associated with the Vagal responses with βSE (another compensatory response) associated with the Syncope responses). Currently, many experts claim that POTS and VVS cannot be co-morbid. This is because, for the most part, they cannot measure both together; therefore, "it must not exist." Yet the two dysautonomias are mediated by two different branches of the autonomic nervous system; three, in fact: 1) Sympathetic Withdrawal (SW, an alpha-adrenergic response) which underlies Orthostatic dysfunction (the "O" in POTS), 2) Parasympathetic Excess (PE; Vagal, referring to Vagus Nerve, is another name for Parasympathetic); and 3) Sympathetic Excess (SE, a beta-adrenergic response) which underlies both the Tachycardia and the Syncope. βSE is associated with the "adrenaline storm" released by the brain to increase cerebral perfusion. The good news is that any or ALL three of these dysautonomias are treatable, simultaneously, and for many patients may be relieved and the patient returned to a normal lifestyle.

Another reason why so many doctors miss Anxiety-like symptoms and confirm it as a psychological condition is because the patient seems normal to them, physiologically. Of course they do! When does the typical doctor assess a patient? When they are resting (sitting or supine). This is section 'A' of the Trends plot (Figure 1), which is summarized in the Resting Baseline Response graph (Figure 2, the patient's response is point 'A' – an average of the five-minutes of rest - is in the middle of the normal area as indicated by the gray shaded region). The vast majority of Anxiety patients are indeed normal at rest. They better be. As our typical patient reports, they have had dozens of doctors over more than a decade of time working very hard to make them normal … at rest! The problem is not at rest. In fact, the P&S nervous systems are rarely at rest, and when the patient is resting, they are typically most active! The problem is when the patient is active, as in the cases of POTS & VVS, while upright, standing, the heart and the P&S nervous systems must fight gravity. There is no time for the P&S systems to rest.

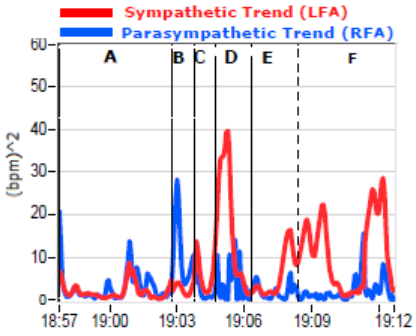

Figure 1: Abnormal Trends Plot of an Anxiety-like Patient. Section 'A' is the Resting Baseline. Parasympathetic and Sympathetic activity (blue and red curves, respectively) are relatively quiet. The breathing challenges ('B' & 'D' with their baselines 'C' & 'E' are within normal limits, see text for more information). The stand challenge 'F' is markedly abnormal. After the first Sympathetic (red) peak (the Autonomic response to the action of standing up), the remainder of the Stand challenge, the quiet stand portion should resemble the Resting Baseline. The additional Sympathetic (red) peaks are the "Adrenaline Storms." See text for more details.

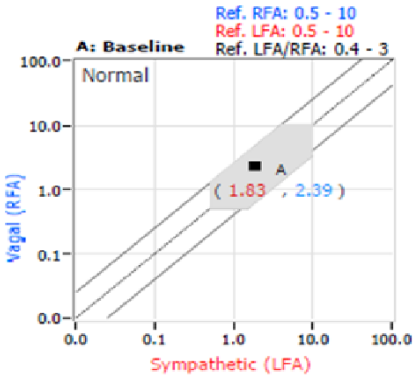

Figure 2: Abnormal Trends Plot of an Anxiety-like Patient. The average response P&S (vertical and horizonal axes, respectively) from the Resting Baseline section ('A') of the Trernds Plot in Figure 1.

An example (Figure 3) of an adult patient with Anxiety-like symptoms is shown below (female – not that gender has a significant effect on the P&S test results). The patient's Trends plot (left) and Resting Baseline graph (center) is shown with a normal adult patient's Trends plot (right). Note that her resting response plot shows a significant amount of Sympathetic activity compared with her resting Parasympathetic activity (the point 'A' is well to the right of the normal gray area). This is reflected in section 'A' of her trends plot with the excess Sympathetic (red) activity. Compare this with the Trends plot from a normal patient (Figure 4).

In a trends plot, the P&S (blue & red curves, respectively) are responses to the standard P&S test: A) Resting Baseline, B) the Parasympathetic challenge of paced breathing, C) a return to baseline, before D) the Sympathetic challenge of a

Pato M, et al., Cardiol Cardiovasc Med 2024
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series of short Valsalva maneuvers, followed by E) another return to baseline, before F) the Stand or postural change challenge (a quick head-up postural change – Stand or Tilt – followed by five minutes of quiet standing or tilt). For the Anxiety-like patient (Figure 3) all of the phases of the test ('A' through 'E') demonstrate more instantaneous activity than that of the normal patient; however, the average responses are within normal limits as indicated, for example, by the Resting Baseline graph for the patient at rest. Only they are out of balance (point 'A' is to the right of the gray area). The Stand portion ('F'), after the initial Sympathetic response to gravity which occurs in the first 15 seconds or so, is actually the only portion of the test that is abnormal (both in absolute value – the instantaneous responses – and on average, see Figure 5, top graph). Yet the patient's Trends plot is filled with all sorts of abnormal P&S activity indicating the struggle of the P&S to maintain normal function. In this case normal cerebral perfusion. In fact, in this case, it takes a relatively similar amount of P&S energy to remain standing as it does to support the stress simulated by the Valsalva challenge. Physiologically, that makes no sense.

The Stand response graph for this patient, with Anxiety-like symptoms, is shown in Figure 5 (top). The excessive Sympathetic (red) activity during the Stand phase indicates βSE (aka, a "Hyperadrenergic" response as indicated in the Stand response plot). The excess Parasympathetic (blue) activity in the abnormal Trends plot is confirmed by the abnormal Stand Response graph to the right as well as "Vagal Excitation). Normally during Stand (see Figure 5, bottom) first the Parasympathetics (the blue portion of the Stand response curve) should decrease from point 'A' (the resting Baseline response) and then the alpha-Sympathetics should increase to the point 'F' (the Stand response), in the middle of the gray (normal) area (see insert, right, bottom). The beta-Sympathetics normally remain quiet. This is much like the brakes and accelerator on a car. To go, first you take your foot off the brake pedal, then you apply your foot to the accelerator. In the case of PE, the "car" is driven with the foot still on the brakes, forcing excess acceleration (βSE) and undue wear and stress on the car, just like the human body. Between the PE indicated in the Stand Response plot and the SE indicated in section 'F' of the Trends plot, VVS is documented.

Because of the PE and βSE, the αSW is masked (due to the fact that a direct measurement of the heart and not the vasculature is part of Cardio-Respiratory monitoring, although of course, the vasculature has a significant influence on the heart). The resulting symptoms of αSW, and in this

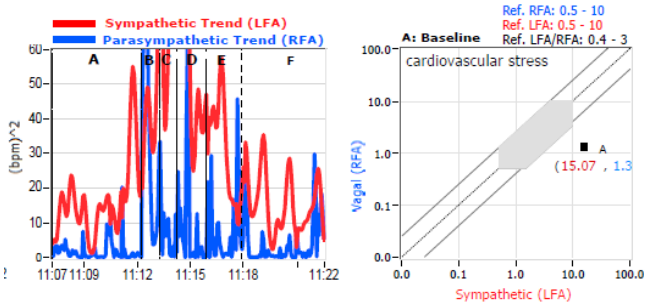

Figure 3: The Trends Plot (left) and Resting Baseline Response Plot (right) of an adult, female patient with Anxiety-like symptoms. See text for details, and Figures 1 & 2 for a description of the graphs.

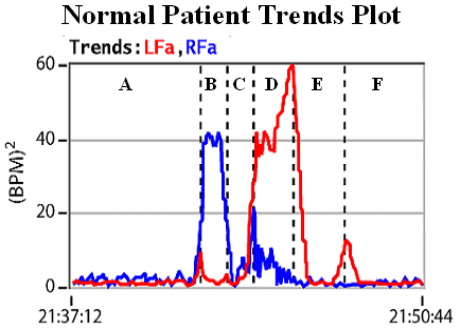

Figure 4: The Trends Plot of a normal adult subject. See Figure 1 for a description of the graph.

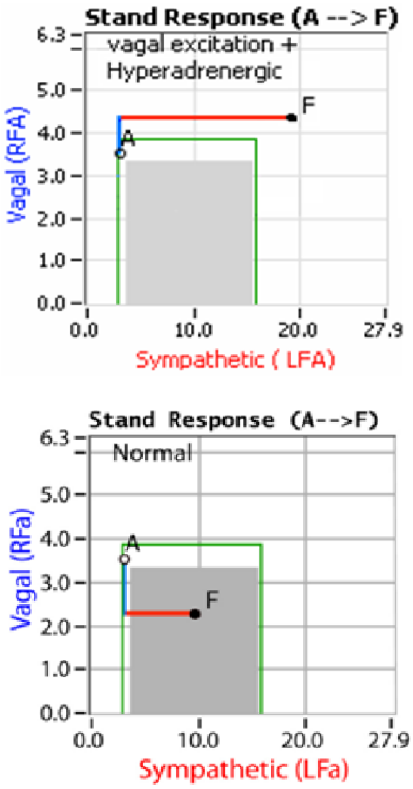

Figure 5: Stand Response Plots of the Aniety-like patient from Figure 3 and of the normal subject subject from Figure 4. Normally the beta-Sympathetic activity during stand is quiet and the alpha-Sympathetic response dominates. However, in the abnormal response the PE and βSE dominate and the αSW is masked. SW is then indicted by the Heart Rate and Blood Pressure responses collected during the P&S or Cardio-Respiratory monitoring test (see Figure 6). See text for details.

Pato M, et al., Cardiol Cardiovasc Med 2024
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Numeric Summary:

	Event	Duration	meanHR	Frequency Domain w/ RESP LFA	RFA	LFA/RFA	BP
A:	Baseline	05:00	67	1.92	3.93	0.49	113 / 79
B:	Deep Breathing	01:00	67	0.83	14.34	0.06	109 / 75
C:	Baseline	01:00	72	3.38	1.81	1.87	105 / 76
D:	Valsalva	01:35	73	40.73	6.77	6.02	129 / 76
E:	Baseline	02:00	75	1.87	2.36	0.79	115 / 83
F:	Stand	05:00	96	3.88	3.78	1.03	104 / 82

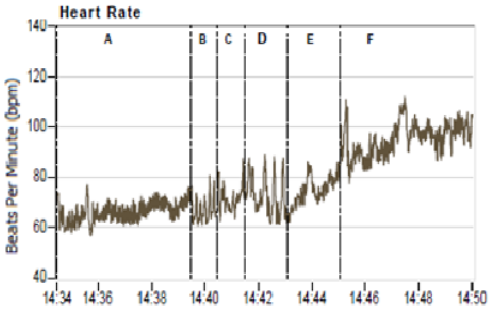

Figure 6: More information from the P&S or Cardio-Respiratory monitoring test. **Table, Left)** a portion of the Summary table documenting the (average) responses for each of the phases of the test, and **Graph, Right)** the Heart Rate plot depicting the cardiogram in response to the test (see Figure 1 and text for the definitions of 'A' through 'F'). The HR response to standing (section 'F') shows a typical pre-clinical POTS response during Stand. See text for details.

case POTS, are documented elsewhere in the HR & BP responses (see Figure 6). The 'O' is the clue. A portion of the Summary table is shown in Figure 6 (left), documenting the (average) responses for each of the phases of the test. The average or mean HR increases upon standing from 67 to 96 bpm, a nearly 30 bpm increase, documenting the Tachycardia associated with POTS. The BP responses drop from Resting Baseline 113/79 mmHg to 104/82 mmHg upon standing, documenting Orthostatic dysfunction pre-clinical Orthostatic Hypotension. Note, there may not be as much of a drop as indicated here, but there is typically an abnormal BP response to stand, even if it is only a weak rise in BP (< a 10% increase over the resting BP). The HR plot (Figure 6, right) depicting the cardiogram in response to the test follows the table and shows a typical pre-clinical POTS response during the Stand ('F') portion of the test. In this case a continued rise in HR after an initial near-normal return to baseline before the onset of the Tachycardia. With these three indications (more information), and experience, we have the confidence to diagnose masked SW and add therapy for Orthostatic dysfunction to the plan.

Restore and Improve Quality of Life

It is not acceptable to make the poor quality of life a new normal; even if the patient cannot remain standing while brushing their teeth in the morning or washing their hair in the shower while standing. For many, Anxiety came on suddenly, apparently from nowhere. You have to go back three to six months before the onset to possibly determine a potential cause. Often the Parasympathetic and Sympathetic (P&S) nervous systems will struggle to maintain normal function even when they are abnormal before they may fail to maintain. There are many possible causes: concussion, psycho-social stress, all sorts of abuses (physical as well as mental), serious viral infections (including COVID-19) and other types of infections (molds, mildews and bacterial), in other words, trauma of some sort. Young women have physically (by volume) smaller hearts than men and older women. Sorry, that is just the way it is. (Notice we say physically, this has nothing to do with the fact that most women are bigger hearted than men; emotionally and nurturing. ☺). Due to the smaller heart, when the brain calls for more blood, the smaller heart does not have the mass to leverage more pressure, so it must leverage more rate to increase blood flow to the brain. This may be why POTS is a common symptom in young women with Anxiety-like symptoms. POTS is, typically, more symptomatic earlier in the day, and may often be missed by testing later in the day. In many other cases Orthostatic Intolerance, or pre-clinical or clinical Orthostatic Hypotension is a common symptom. All are due to an underlying αSW which confounds and adds complexity to the diagnosis and treatment of the common co-morbidity PE. Again, all of these autonomic dysfunctions are treatable and in many cases are relieved; most with supplements and lifestyle therapies, often accelerated by short-term, low-dose pharmaceutical therapies. To help healthcare providers, more information is needed. P&S monitoring is more information. As shown in the graphs and tables above, P&S monitoring may document if VVS is involve with POTS requiring additional therapy for the PE. This "takes the foot off the brakes" so that "the over-acceleration," the βSE, may normalize organically, which in turn will relieve Tachycardia and other Sympathetically mediated symptoms; organically (assuming no end organ-effects). In other words, by taking the foot off the brakes, the need to accelerate harder is relieved, which in turn, relieves stresses on the engine and the brakes. P&S monitoring is able to document all P&S dysfunctions underlying Anxiety-like symptoms in a single test.

Diagnostic Summary

To summarize, the three separate parts of the P&S systems that may be involved and all at the same time (especially in more serious and complex cases) are:

- 'O' = SW, an α-adrenergic dysfunction,
- 'V' = PE, a Vagal dysfunction,
- 'T' & 'S' = SE, an β-adrenergic dysfunction.

Pato M, et al., Cardiol Cardiovasc Med 2024
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SW & PE are associated with the following: lightheadedness, cognitive dysfunction or "brain fog", and frequent headache or migraine, sleep difficulties, fatigue, exercise intolerance, difficult to control BP, blood glucose, hormone level, or weight, difficult to describe pain syndromes (including CRPS), unexplained arrhythmia (palpitations) or seizure, GI disturbance, temperature dysregulation (both response to heat or cold and sweat responses), sex dysfunction, and symptoms of depression or Anxiety, ADD/ADHD, OCD, as well as high-functioning Autism (these last five disorders are persistent ways of working to restore proper cerebral perfusion). The "brakes and accelerator" model is the better way to consider the P&S (or autonomic) nervous systems. The brakes represent the Parasympathetics and the accelerator represent the Sympathetics. The "see-saw" model as taught in Medical School is still included and addresses resting conditions. Typically, at rest or under normal conditions, a foot is either on the brakes and off the accelerator or vice versa; there is the "see-saw." For example, as mentioned above, upon standing, first the Parasympathetics should decrease and then the Sympathetics should increase. This is much like the brakes and accelerator on a car. To go, first you take your foot off the brake pedal, then you apply your foot to the accelerator. Upon releasing the brakes, the car already begins to roll (accelerate) minimizing and potentiating the amount of acceleration, stress, and wear, required to normally reach speed.

However, for abnormal responses, the "see-saw" model often fails. For example, if the brakes are not released, and the accelerator is depressed, the car will still go, but it takes more acceleration. In effect, the acceleration is amplified (even though the car is not going as fast because the brakes are engaged), and so are the results of acceleration; the symptoms, including Anxiety-like symptoms. This is the effect of PE, causing secondary βSE which is the "adrenaline storm" or β-Sympathetic stimulus of the heart meant to increase blood flow to the brain and everywhere above the heart. To extend the brake and accelerator analogy, SW (an abnormal α-Sympathetic response) is like hitting the accelerator and abnormally low amounts of gas gets to the engine, so either the engine barely goes (fatigue, brain-fog, sleep difficulties, memory or cognitive dysfunction, vision effects, ringing in the ears, lightheadedness, taste or smell disorders, etc.) or the engine stalls (fainting or you feel like fainting and you have to sit or lay down). In the case of αSW, blood pools in the feet, ankles and lower legs, causing poor coronary (heart) and cerebral (brain) perfusion. These symptoms are also caused by PE. With αSW, not enough blood is returned to the heart and therefore is not available to send to the brain. With PE, the heart is not permitted to send enough blood to the brain due to vasodilation or inefficient pumping, regardless of whether there is enough coming from the feet. PE, however, amplifies Sympathetic activity, like amplifying acceleration or over-revving the engine. In the body, the results of amplified acceleration (amplified β-Sympathetic activity) may be Anxiety; Inflammation; allergic or histaminergic over-reactions, amplified pain; Hypertension or difficult to control BP; difficult to control blood sugar or hormone-levels; tachy-arrhythmia; amplified stress responses; and more. All of these are Sympathetic symptoms, and some may be critical in nature. More specifically, these are β-Sympathetic symptoms. As indicated above, there are two Sympathetic branches in the body: one branch, the α-Sympathetic branch, which primarily controls and coordinates the vasculature outside the thorax (the rib cage); the other branch, the β-Sympathetic branch, which primarily controls and coordinates the heart and lungs (inside the rib cage). The β-Sympathetic symptoms may be secondary to either or both SW (an α-Sympathetic response) or PE because they tend to be compensatory in nature. Regardless of the mechanism (SW or PE or both), not enough blood gets to the brain, resulting in the β-Sympathetic symptoms due to the β-Sympathetic response attempting to stimulate the heart to pump more. If the physician does not think to consider the β-Sympathetic responses as secondary, attempting to treat only the β-Sympathetics or treating them as the primary, may exacerbate the conditions because the body is working to compensate and may find ways to defeat the therapy to properly perfuse the brain. Ultimately, this may cause the potentially critical nature of βSE (heart attack or stroke) to become a self-fulfilling prophecy.

Therapy Options

In either case (SW or PE or both), proper daily hydration is required. This includes a minimum of 64 oz of water taken throughout the day with an additional 5.5 g of electrolytes dosed every two hours throughout the day. The electrolytes may be sodium from salt (1 tablespoon, including flavored salts) if the patient's BP is normal to low, less than approximately 160/90 mmHg, history dependent. If BP is high, then the electrolytes may be potassium from (bananas or prunes, for example). For days with more activity (loosing water and electrolytes through sweat for example) or in women days of their period, more water is required, up to 96 oz with 8.25 g of electrolytes. For SW, low-dose, oral vasoactive therapy (*e.g.*, Midodrine, 2.5 mg tid, history dependent; an α-1 Sympathetic agonist or stimulant) typically relieves the β-Sympathetic symptoms organically, after relieving any Orthostatic dysfunction caused by the SW. In other words, vasoactive therapy helps to relieve blood pooling in the lower extremities, moving the blood to the abdomen, helping the heart pump blood to the brain, thereby restoring proper brain perfusion. This in turn prevents the need for adrenaline storms, thereby relieving the β-Sympathetic symptoms, like tachycardia, stress, and inflammation. Checking to "see if gas is getting to the engine" (αSW) and treating to ensure it does (*e.g.*, unclogging the fuel filter or fuel line), relieves βSE organically (reducing the amount of acceleration needed), ultimately relieves the β-Sympathetic symptoms. Of course,

Pato M, et al., Cardiol Cardiovasc Med 2024
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this process takes time. It is not a quick fix. In fact, it may take up to 24 months, depending on the patient's history, including daily stress levels. The oral vasopressor helps to speed the recovery as much as possible, but not everyone responds to it. The first line alternate therapy is 600 mg, tid, r-Alpha-Lipoic Acid. Compression garments are also recommended in the interim. Still the oral vasopressor does not help to speed recovery all that much. To use another analogy: the P&S Nervous Systems are like a pendulum, if to correct it you hit it hard or fast, you knock the pendulum off its hinge and create more problems. Therapy must be slow, gentle, easy nudges over time, or for another analogy, it is like stopping a bad habit and establishing and maintaining a good habit.

Similarly, checking to see if the brakes are "on" (PE) and treating to release the brakes may resolve all of the above Sympathetic abnormalities, including Anxiety-like symptoms. Relieving PE (releasing the brakes), relieves βSE (reducing the amount of acceleration needed), ultimately relieves the β-Sympathetic symptoms. Low-and-slow exercise is the primary alternate therapy for PE. PE may be relieved pharmaceutically with low-dose anti-cholinergic therapy (very, low-dose antidepressant therapy; *e.g.*, 10.0 mg Nortriptyline, qd, 12 hrs before waking, as it also helps to pattern sleep). Of course, this process also takes time. Again, it is not a quick fix. In fact, it again may take up to 24 months. Unfortunately, most autonomic tests only test total autonomic activity and are not able to independently and simultaneously measure the two autonomic branches without assumption and approximation. Even tilt table is often unrevealing because of complications and its inability to independently and simultaneously differentiate P from S without assumptions, approximations, chemicals or ignoring symptoms until they are so bad that the assumptions are valid. However, even then, as soon as therapy is implemented the assumptions are no longer valid and therefore Tilt-testing is no longer revealing. As an aside, for VVS, the stress and anxiety (Sympathetic stimuli) caused by the tilt table itself temporarily "cures" VVS (balances the Parasympathetics), leaving the physician with no diagnosis to treat and believing that the patient is normal.

Summary

The good news with P&S monitoring is that all three dysautonomias (SW, PE & SE) are treatable, all simultaneously. Again, however, it is not "quick fix" it may take up to 24 months. Therapy must be low-and-slow. Again, like correcting a pendulum, or essentially breaking one or more "bad habits" and establishing good habits, never fast. Therapy may be both pharmaceutical, and for those that have been put on high doses and are desensitized, we have developed non-pharmaceutical therapies. The main issue is that the heart is being made to act as if it is deconditioned by the P&S nervous systems and must be reconditioned. At the same time the lower vasculature must be re-integrated with the heart. Once all of this is done, symptoms are relieved and Quality of Life is restored or improved, until some other clinical event. The *only* reason for maintenance dosing of any kind, let alone life-long therapy, is if there is some remaining end-organ dysfunction that will continue to pull the P&S systems out of balance. A summary therapy plan for the autonomic dysfunction associated with Anxiety-like symptoms is included below.

- First, suppress any β-1 Sympathetic, the accelerator, stimulation with low-dose β-blockers, such as Propranolol or Nadolol. This is typically short-term and low dose, to reduce and prevent palpitations and rapid HR and to prevent additional fatigue or exercise intolerance, until the nervous system is re-trained to respond normally upon standing. Typically, the patient will self-wean.
- Second is low-dose anti-cholinergic treatment with low and slow exercise to relieve PE. The anti-cholinergic therapy also helps to relieve sleep difficulties. If the brain is poorly perfused during the day, while the head is higher than the heart, when the patient lays down the brain and the heart are at the same level. In this way the brain is now properly perfused and "wakes-up and wants to play." The patient wants to sleep. This is not insomnia. Patterning sleep helps with many other symptoms as well.
- Third, stimulate α-1 Sympathetics, the accelerator, with oral vasoactives, fluids, electrolytes, compression garments, and r-Alpha-Lipoic Acid. The oral vasoactives are also often short-term. All of this is to relieve the brain-fog, cognitive and memory difficulties, lightheadedness, fatigue, Orthostatic dysfunction (including POTS or Orthostatic Hypotension), etc., associated with Anxiety-like symptoms.

Typically, these first three steps are administered simultaneously. Last, if blood volume remains an issue (*e.g.*, water and electrolytes are not sufficient), then low-dose volume expanders are recommended (*i.e.*, Florinef or Desmopressin).

Treating Sympathetic issues as the primary autonomic dysfunction typically exacerbates the patient's condition, including making them more difficult to manage, or they do not tolerate the therapy. Granted mortality risk(s) need to be addressed, such as high resting BP or high Standing HR, but recognize that these may be secondary and typically are relieved with the relief of SW or PE. SW or PE therapy must be "low and slow" with SW often the first and most difficult dysautonomia to fully correct. Ultimately, Anxiety-like symptoms are blood flow issues that are caused by P or S dysfunction(s). Without testing for both P&S activity, independently and simultaneously, at rest and in response to challenge, the best that may be offered the patient is a guess

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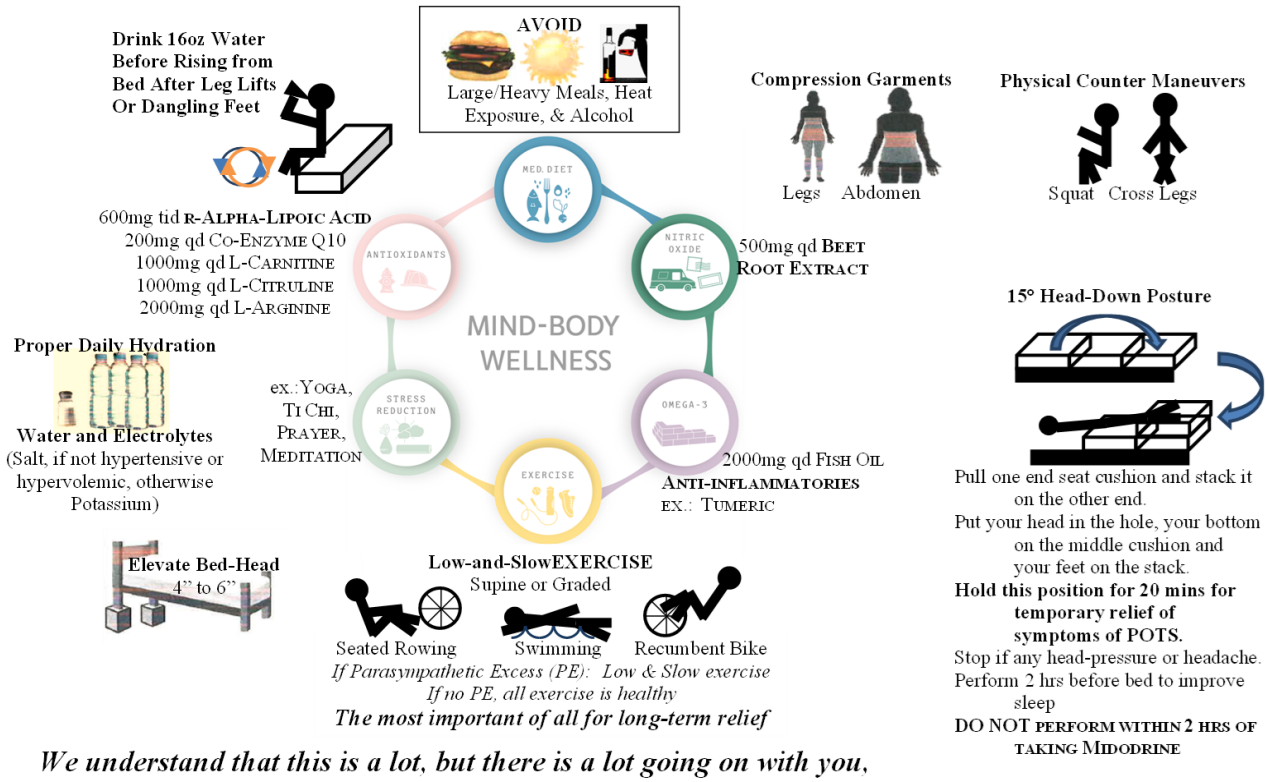
and a bad guess at that. This is the reason why the general sentiment towards autonomic dysfunction has moved to a life-long management: 1) to keep it a research project and 2) to sell more drugs. Without a clear, objective, quantitative measure of the Parasympathetic nervous system, and therefore a clear, objective, quantitative measure of the Sympathetic nervous system, patients are being done a dis-service, as evidenced by the millions of patients taking matters into their own hands and still diligently seeking more information. P&S Monitoring is the more information.



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