



Summary Review: The Dysfunctional Autonomic Nervous System in ME/CFS

And some tips that might help address these problems

By Charlotte Stephens, 24th January 2018.

Two research studies recently reported similar findings relating to the autonomic nervous system in people with ME/CFS. Both related to sleep and build on existing evidence suggesting that a dysfunctional autonomic nervous system (also known as dysautonomia) is perhaps creating or exacerbating some of the symptoms that may be associated with ME/CFS.

In this ME Association summary review, I hope to explain:

1. the autonomic nervous system and how it functions
2. the latest research findings in relation to sleep, and,
3. suggest some things you can do to help address these problems.

Altered autonomic nervous system (ANS) functioning has been frequently reported in patients with ME/CFS (Johnson, 2017). Symptoms that are related to ANS dysfunction in ME/CFS include:

- Dizziness, light-headedness and feeling faint on standing (postural hypotension)
- Orthostatic intolerance (being unable to stand for long periods)
- Palpitations
- Cold hands and feet
- Irritable bladder symptoms
- Gastric and irritable bowel type symptoms – including nausea

A condition known as postural orthostatic tachycardia syndrome (POTS) also occurs in a sub-group of people with ME/CFS.

Something called heart rate variability (HRV) – see below – can be used as a measure of autonomic function and this was used in the two studies published last month.

Although the studies were small, they concluded that there is an apparent dysfunction, or imbalance, in the ANS during sleep and when awake, with one study looking at the effects before and after an exercise and cognitive challenge.

Each study concluded that HRV in CFS is lower than controls during sleep, suggesting higher sympathetic nervous system activity and lower parasympathetic nervous system activity (see below).

Note: for the purposes of this review, we might regard high sympathetic nervous system activity as 'bad', as it means a higher state of arousal, and the body being on a heightened state of alert, which if sustained, can produce symptoms associated with ME/CFS.

1. What is the ANS (Autonomic Nervous System)?

The nervous system spans the whole body, connecting all our organs and tissues with each other and the brain, sending messages between them.

It is split into two systems: The central nervous system and the peripheral nervous system.

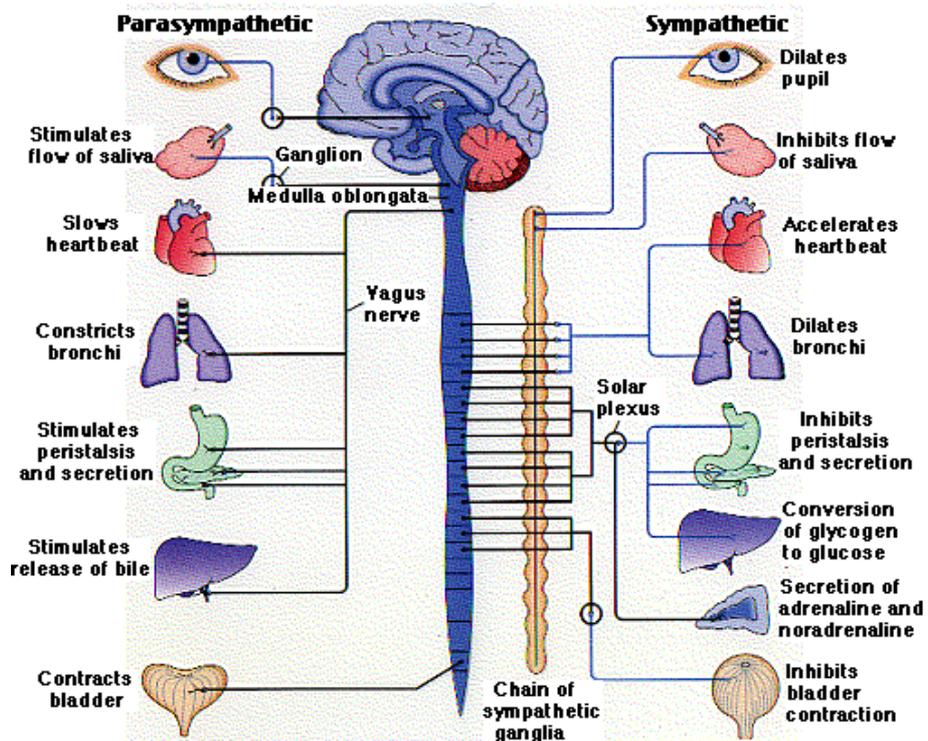
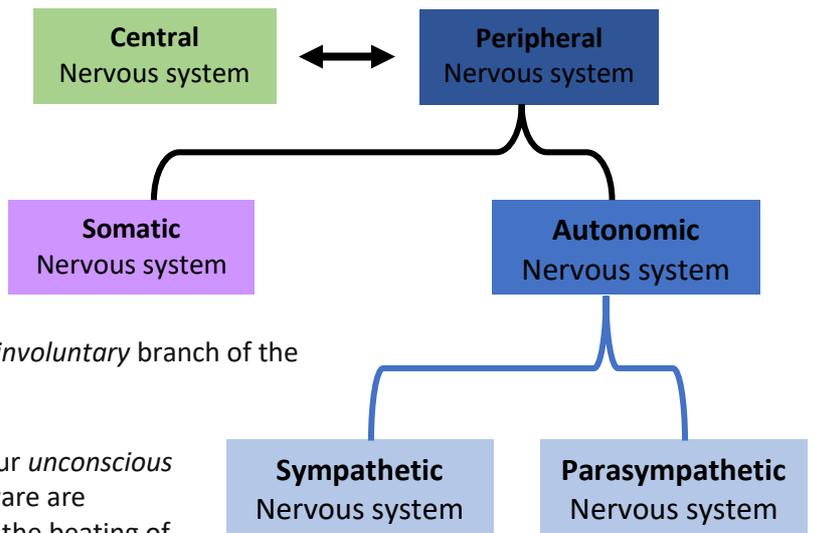
The autonomic nervous system (ANS) is the *involuntary* branch of the peripheral nervous system.

Involuntary means that it controls most of our *unconscious* actions, that, most of the time, we aren't aware are happening; such as breathing, digestion and the beating of our heart, so it's like an auto-pilot system.

However, it is also possible to take the system out of auto-pilot and into manual, as we can control the actions of the ANS to some extent, and with practise (I'll return to this later).

The ANS has influence over muscles and glands throughout the body and controls a whole range of things, including heart rate, breathing, salivation, digestion, perspiration (sweating) and urination.

The ANS is further subdivided into two opposing sections; the sympathetic and the parasympathetic nervous systems. These two divisions have a sort of yin-yang relationship; they both act on the same parts of the body but produce completely opposite effects.



The sympathetic nervous system (SNS) likes to speed everything up (get you 'hyped') and is best known for stimulating the 'flight or fight' response, having effects such as increased heart rate, increased breathing, dilated pupils, slowed digestion, and increasing blood-flow to the muscles in preparation for movement.

On the other hand, the parasympathetic nervous system (PNS) likes to calm you down (relax you) and is known for the 'rest and digest' response, having opposite effects to the SNS, such as slowing your breathing, reducing your heart rate, constricting pupils, and encouraging digestion.

Personal side-note on pupil dilation: I find this effect particularly interesting as, when I am feeling a crash coming on, my family have often mentioned how big (dilated) my pupils have gone, and it is a tell-tale sign that I am going downhill. This makes sense to the theory that my SNS is in overdrive. It would be interesting to see how many others have noticed this.

When in balance, these two systems work together well in the body. However, they are selfish systems as when one is working, the other one cannot; one must be 'switched off' in order for the other to work – they cannot both work at the same time.

Understandably, the sympathetic nervous system is very energy demanding, whilst the parasympathetic nervous system, is energy conserving.

There's a good YouTube video that explains the ANS in a simple, fun (but fast!) way, here: <https://www.youtube.com/watch?v=71pCilo8k4M>

Interestingly, the ANS stems mainly from the ganglion, an area which has been mentioned in M.E. research as being dysfunctional; there is a hypothesis based on post mortem research that inflamed neurons in the dorsal root ganglion are interfering with proper autonomic nervous system functioning.

MRI studies have found that symptoms of fatigue in CFS subjects were associated with reduced responsivity of the basal ganglia (Unger *et al.* 2012; Miller *et al.* 2014).

A post mortem of a patient with M.E. revealed inflammation in and around the dorsal root ganglion, with the authors hypothesising that dysfunction of the sensory and the autonomic nervous system may lead to abnormal neural activity and explain some of the symptoms of M.E. (Lacerda *et al.* 2010).

What is Heart Rate Variability (HRV)?

Heart rate variability (HRV) is the variation in the *time between each heart beat* and can be measured via an ECG or some chest strap heart rate monitors.

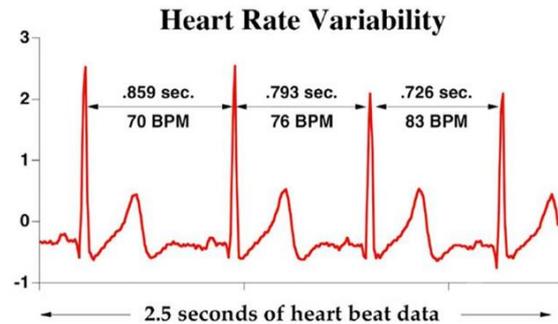
Your heart rate is not meant to stay the same speed all the time; it changes depending on your activity and emotions.

HRV is a very good measure of the efficiency and performance of the cardiovascular system (Papaioannou *et al.* 2013).

Having high HRV is preferable as it means your body can efficiently adapt and change your heart rate depending on your activity.

Studies suggest that people who have a higher HRV are healthier and live longer with less risk of disease.

Hillebrand *et al.* (2013) found that low HRV is associated with a 32-45% increased risk of a cardiovascular event.



Heart rate variability may also be a marker of how well your body can handle stress. This is because it can act as a measure of the relative activity of the sympathetic and parasympathetic divisions of the ANS.

Meeus *et al.* (2013) measured HRV in CFS patients and found that *increased sympathetic activity* was present in CFS patients at night (not good- we don't want to be 'hyped up' and 'on alert' when trying to sleep!).

ANS problems and ME/CFS

Many studies have found the ANS to be dysfunctional, or 'out of balance' in ME/CFS patients (called 'dysautonomia'). Robinson *et al.* (2015) found evidence of dysautonomia in almost 90% of CFS patients.

ANS imbalance can also impact the length, type and quality of sleep, with evidence suggesting that reduced HRV (showing increased sympathetic activity) in patients with ME/CFS is most prominent during sleep (Boneva *et al.* 2007).

An overactive sympathetic system has been associated with poor sleep, cognitive decline, inflammation and increased pain, and so it could play a role in many of the symptoms of ME/CFS (Fisher *et al.* 2010) – see table 1 below.

One research group said, "We have studied autonomic function in CFS for some time and our findings clearly indicate a *loss of integrity* in stress-responsive systems in CFS. Patients with this condition are *hyper-responsive* to challenges arising both from within the body and from the environment. Even while asleep, their stress-responsive neural systems are on *high alert*, signalling that it is not safe to relax." (Beaumont *et al.* 2012).

ME/CFS patients tend to have *reduced parasympathetic activity*, and *increased sympathetic activity*, known as "sympathetic nervous system predominance" (Martinez *et al.* 2014). This same ANS dysfunction is seen in healthy people after engaging in acutely fatiguing tasks, and the *lack of parasympathetic activity* appears to correlate to feelings of *fatigue*. The difference is that in CFS, the ANS dysfunction happens after *much lower levels of stress or activity* (Tanaka *et al.* 2015).

In simple terms, people with ME/CFS are hyper-sensitive to anything from infections and pain within the body to stimuli outside the body, such as noise, heat or emotional stress. The body is stuck in a high-alert – 'we need to defend ourselves from all threats' – mode (otherwise known as the 'fight or

flight response’, stemming from the sympathetic nervous system).

Symptoms of Sympathetic dominance	
<ul style="list-style-type: none"> • Excessive Fatigue • Exercise intolerance • Nausea/ poor appetite • Constipation • Poor Digestion/indigestion • Anxiety/nervousness • Shallow breathing • Fast/slow/irregular heart rate • Low blood pressure • Light-headedness/dizziness upon standing • Weakness • Insomnia/ Poor quality sleep • Increased agitation/irritability • Concentration/memory problems 	<ul style="list-style-type: none"> • Increased muscle tension • Night sweats • Decreased Libido • Increased inflammation • Increased susceptibility to infections • Temperature regulation problems • Cold hands/feet • Hyper-sensitivity (to light/noise) • Headaches • Tremors • Frequent urination • Chronic pain • Joint pain • Body aches

Table 1 – Symptoms of sympathetic nervous system dominance

Naturally, being on a constant state of high alert, quickly drains the body of energy and can result in other problems, such as gastrological symptoms, as digestion is not a priority in this state. The sympathetic system puts many organs and processes into overdrive and deprives other areas of blood and oxygen, so this is not an ideal state to spend most of your time in!

“Sympathetic nervous system predominance is common in chronic fatigue syndrome and measures should be taken to regain autonomic balance” Martinez et al. (2014).

2. Overview of the latest research on ANS and sleep

The First Paper (by Cvejic et al. 2017):

This study explored changes in autonomic functioning, sleep, and physical activity during a period of post-exertional symptom exacerbation, induced by physical or cognitive challenge in participants with chronic fatigue syndrome (CFS).

Thirty-five participants with CFS (meeting the Fukuda definition) reported fatigue levels 24hrs before, immediately before, immediately after, and 24hrs after the completion of a physical (stationary cycling) or cognitive (simulated driving) challenge.

Participants also provided ratings of their sleep quality and duration for the night before, and after, the challenge. Continuous ECG and physical activity was recorded from 24hrs prior, until 24hrs after, the challenge.

To be recruited to this study, the CFS patients were required to have a steady level of symptoms, with no major fluctuations in severity, as well as a good sleep schedule (consistent sleep and rise times and minimised daytime napping).

Medications affecting autonomic functioning (including beta-blockers and corticosteroids), or any other contraindications (untreated anxiety, uncontrolled cardiovascular complaints) were exclusionary.

Participants were only allowed to take part in the physical challenge if they were shown able to carry out regular low-intensity exercise, without symptom exacerbation, and were physically capable of performing moderate-intensity aerobic exercise for at least 25 min. Although this was clearly in the best interest of the health of the participants, this may mean that this 'challenge' was within their activity levels and did not bring about a big enough PEM response to observe noticeable differences.

The paper even comments on the suitability of their participants: "although experiencing significant impairment, they may have been more functional than others who are unable to undertake outpatient treatment or tolerate challenge protocols. It is possible that individuals with more severe fatigue and functional disability would have greater symptom exacerbation in response to challenges, accompanied by more prominent alterations in autonomic parameters".

In other words, it seems reasonable to assume that monitoring a more severely-affected cohort of patients would show even greater autonomic dysfunction and dysautonomia.

Both physical and cognitive challenges induced an immediate increase in fatigue, which remained elevated 24hrs post-challenge. And, after completing the challenges, participants spent a greater proportion of the day lying down, but did not experience significant changes in sleep quality or sleep duration.

Heart rate and heart-rate variability (HRV) were found to be reduced slightly post-challenge in the CFS group. Everyone's HRV should *increase* when they're asleep, compared to when they're awake, which was the case for the patients with CFS. However, the *amount of increase* in the HRV between wake and sleep was significantly *reduced* after completing the challenge, suggesting reductions in nocturnal parasympathetic activity during the period of post-exertional malaise (PEM).

High HRV is associated with better quality of sleep, but HRV during sleep was reduced post-challenge or during the period of PEM. However, CFS patients did not report a significant reduction in quality of sleep post-challenge to accompany the drop in HRV. The authors comment, "this might reflect a lack of sensitivity in subjective sleep quality measures". It could also be that because these patients were mild, it may not have induced significant PEM and so didn't affect their quality of sleep.

The paper concluded: "Preliminary evidence of reduced nocturnal parasympathetic activity, and increased periods of inactivity, were found during post-exertional fatigue in a well-defined group of participants with CFS. Larger studies employing challenge paradigms are warranted to further explore the underlying pathophysiological mechanisms of post-exertional fatigue in CFS."

The second Paper (by Orjatsalo et al. 2017):

This study looked at the nocturnal (night-time) cardiac autonomic nervous system (via heart-rate variability (HRV)) in different sleep stages in 8 patients (meeting the 2015 Institute of Medicine

ME/CFS diagnostic criteria) and 8 “tired” controls. HRV, blood pressure and heart rate were studied in all sleep stages.

The amount of *sympathetic* activity was *higher* for patients with CFS in all sleep stages compared to controls. The amount of *Parasympathetic* activity was *lower* in deep sleep in the patients with CFS than for the controls. Patients with CFS had *higher* overall nocturnal mean *Blood Pressure* and *lower heart rate* than controls.

The paper concluded: “The results suggest a nocturnal dysfunction of the cardiac ANS in CFS, presenting as *lower parasympathetic tone* in deep sleep and *higher sympathetic tone* asleep.”

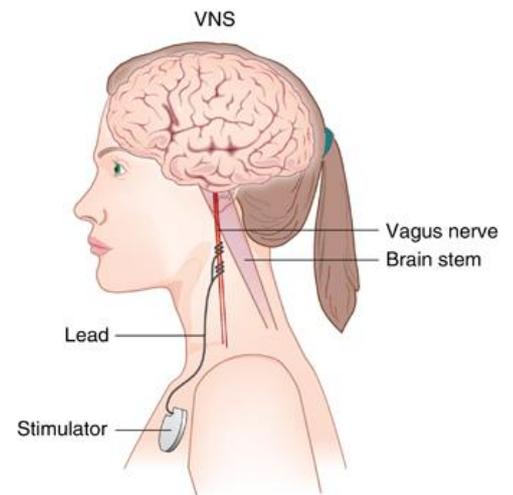
3. So, what can we do about it?

Unfortunately, there is no drug or ‘quick fix’ to help restore a state of balance (or homeostasis) within the autonomic nervous system that might help relieve some of the symptoms we have seen are associated with dysautonomia.

The Vagus nerve is a large nerve in the back of the neck that controls parasympathetic activity (the ‘rest and digest’ system).

People with CFS and other chronic illness are said to have ‘low vagal tone’ and by increasing this, it is possible that you can increase your parasympathetic activity and help towards reducing symptoms.

There are some medical innervations designed for resetting the ANS by stimulating the Vagus nerve, by surgically implanting an electrode in the neck region, or by applying an electrode to the surface of the ear (Clancy *et al.* 2014), which are reported to have been successful in several disorders. However, these techniques are invasive, not widely used and are currently not on offer to patients with ME/CFS (Johnson, 2014).



There are several self-help measures that have been reported as being helpful ways to increase vagal tone, which in themselves seem simple, although incorporating them as a regular part of your life may prove difficult.

These mainly involve techniques that induce the relaxation response which, over time, affects autonomic nervous system functioning (Nick Earle, 2017). They are summarised below.

Whilst good breathing techniques and relaxation may well be helpful, it must be noted that there is currently no research evidence to indicate that increasing vagal tone is a safe and effective form of treatment for ANS dysfunction in ME/CFS.

And some of these approaches (e.g. taking regular cold showers) could produce an exacerbation of ME/CFS symptoms. So, if you want to try some of these approaches, please take medical advice first.

Self-help measures aimed at improving parasympathetic activity (vagal tone)

1. **Deep diaphragm breathing** (belly breathing) – Deep, slow breathing increases the sensitivity of the nerves that activate the parasympathetic nervous system (PNS). Breathe deep so that your belly rises and falls, keeping your in and out breaths the same length, aiming for about 5-6 breaths per minute (there is a video on this below).
2. **Mindfulness/Meditation** (Black *et al.* 2015) – activates the PNS.
3. **Gentle aerobic exercise** (Yoga/Tai Chi/ swimming) (Chang *et al.* 2008) – Not only does this stimulate the PNS, it also encourages deep breathing.
4. **Humming or singing** – stimulates the muscles at the back of the throat to activate the Vagus nerve. Even more reason to sing in the shower or the car or hum your favourite tune!
5. **Supporting a healthy gut** (diet) – The presence of healthy gut bacteria **has been claimed to** create a positive feedback loop through the Vagus nerve, increasing its tone. Probiotics, animal protein and essential fats (omega 3 and 6 – found in oily fish, avocados, olive oil, nuts) **have all been claimed to** decrease an overactive sympathetic nervous system (SNS) and stimulate the Vagus nerve. Also, ensuring your diet is sufficient in B-vitamins, Calcium, Magnesium and Zinc, to support nerve function **is said to** help. Cutting down on or eliminating caffeine and alcohol is also important as they both stimulate the SNS.
6. **Muscle Relaxation** – By actively relaxing your muscles, through ‘progressive muscle relaxation’ techniques or with a warm bath, helps stimulate the PNS by switching off the SNS. Relaxed muscles send messages to the brain, telling it that nothing is alerting the body to a threat, so it can relax.
7. **Massage and Acupuncture** – Certain pressure points in the feet, neck and ears are believed to manually stimulate the Vagus nerve (da Silva *et al.* 2014) and create a sense of relaxation.
8. **Cold** – Counterintuitively, taking a cold shower, splashing cold water on your face, drinking cold water, or being in a cool environment, are thought to stimulate your Vagus nerve and PNS.
9. **Sunlight** – Being out in the sunlight produces a chemical called Alpha-MSH, which activates the Vagus nerve (Ottani *et al.* 2010) and PNS.
10. **Laughter!** – Stimulates the Vagus nerve, is also believed to be good for cognitive function and it releases endorphins (the ‘feel-good’ hormones).



Here are some videos on Vagus nerve/ parasympathetic system stimulation:

<https://www.youtube.com/watch?v=tY8STCSEB10>

https://www.youtube.com/watch?v=v4b_SdLj6Wc

<https://www.youtube.com/watch?v=RSYzleoQQBs>

And here are some gentle Yoga videos:

<https://www.youtube.com/watch?v=qDlcJY37LwY>

<https://www.youtube.com/watch?v=7UilFRFJ-aM>

Additional information from the ME Association

The ME Association has information leaflets covering most aspects of ANS dysfunction in ME/CFS. Click the links below and you will be taken to our online shop:

- [Cold hands and feet](#)
- [Orthostatic intolerance in ME/CFS](#)
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