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*Communication*

# The Adapted Autonomic Profile (Aap) Home-Based Test for the Evaluation of Neuro-Cardiovascular Autonomic Dysfunction

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## Abstract

Autonomic dysfunction is an increasingly recognised complication in chronic neurological conditions such as Parkinson's disease , and other medical conditions, including diabetes mellitus, chronic fatigue syndrome, fibromyalgia and recently Long Covid. Despite laboratory-based tests to evaluate normal and abnormal autonomic function, there are no home-based tests to record neuro-cardiovascular autonomic responses to common stimuli in daily life that are dependent on the normal functioning of the autonomic nervous system. We have developed an adapted blood pressure/heart Autonomic Profile (aAP) that can be used by an individual independently and repeatedly in a domiciliary setting to determine the physiological and symptomatic response to standing, food, and physical and mental (cognitive, emotional) activities. The aAP aids separating autonomic failure (often irreversible) from autonomic dysfunction. This helps the individual and attending healthcare professional understand the relationship between symptoms and common triggers in daily life, and informs on self-management in debilitating conditions such as the postural tachycardia syndrome (PoTS) and Long Covid.

**Keywords:** autonomic failure; lean test; active stand; long covid; Post-COVID-19 condition

## Introduction

The autonomic nervous system (ANS) innervates the smooth muscle of all organs, including the heart, blood vessels and various glands. It is responsible for organ function and mediating involuntary internal homeostasis, to include control of blood pressure (BP), heart rate (HR) and

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thermoregulation. This is unlike the somatic nervous system, which largely is under volitional control. The ANS works along with the hormonal and immunological system to respond to external and internal stimuli and ensure internal equilibrium is maintained as much as possible to enable the stable functioning of the various organ systems.[1] The central ANS centres are in the brainstem, hypothalamus and cerebrum; the peripheral ANS includes the sympathetic and parasympathetic nervous systems, influencing their actions on body functions via transmitters such as acetylcholine and noradrenaline.

Autonomic dysfunction (AD) can result from damage to the ANS or can be idiopathic, episodic or unexplained in some cases [1] (Table 1). Long Covid is a relatively new condition and AD is reported to be present in at least a third of the individuals.[2 3] There is a considerable overlap with Myalgic Encephalitis/ Chronic Fatigue Syndrome (ME/CFS) where an essential feature is Postural Tachycardia (PoTS).[4] The other common symptoms of Long Covid (breathlessness, gastrointestinal symptoms and pain) can be explained by the underlying dysautonomia, which is commonly seen in most post-viral syndromes.[3]

**Table 1. Classification of some autonomic conditions and common symptoms of or related to autonomic dysfunction**

| Cause | Conditions | Symptoms |
|---|---|---|
| Structural central | Multiple System Atrophy (MSA)<br>Parkinson's Disease (PD)<br>Acquired Brain Injury (ABI)<br>Spinal cord injury | *Cardiovascular:* Orthostatic hypotension, palpitations, postural tachycardia, dizziness, presyncope/ syncope, facial flushing,<br>*Systemic:* Fatigue, exercise intolerance<br>*Neurological:* Brain fog, vertigo, dizziness, headache, sleep problems<br>*Gastrointestinal:* Xerostomia, nausea, vomiting, dysphagia, irritable bowel syndrome constipation/diarrhoea<br>*Genitourinary:* Urgency, frequency, polyuria, impotence<br>*Musculoskeletal:* Joint pain, muscle pain<br>*Skin/ vasomotor:* flushing, piloerection, excessive sweating, intolerance to heat/cold<br>*Eyes:* Pupillary dilation, light sensitivity, hypolacrima |
| Structural peripheral | Diabetes Mellitus<br>Autonomic neuropathy such as due to amyloidosis<br>Familial dysautonomia | |
| Idiopathic | Chronic Fatigue Syndrome<br>Fibromyalgia<br>Migraine<br>Autonomic mediated Syncope (AMS)<br>Postural Tachycardia Syndrome (PoTS)<br>Irritable Bowel Syndrome<br>Long Covid | |

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Many of the tests used for ANS evaluation are based on cardiovascular reflexes triggered by performing specific provocative manoeuvres in a controlled environment. Stimuli that alter BP or HR, such as in response to standing or passive tilting on a tilt table, and in response to the Valsalva manoeuvre, isometric exercise, cutaneous cold or heat, mental arithmetic, and deep breathing activate ANS responses that can be accurately measured.[5 6] Techniques such as measuring heart rate variability (HRV), plasma noradrenaline and adrenaline levels, sudomotor testing and microneurography test specific aspects of autonomic function.[6 7]

The neuro-cardiovascular autonomic response to postural change are assessed in various ways, in addition to standing upright. The active stand or NASA lean test measures HR and BP while standing for 10 min.[8] Measurements are made first while in the supine position. When upright, due to gravitational change, blood is redistributed to the lower extremities, which decreases venous return and cardiac stroke volume. Physiological compensatory responses through the ANS are activated to maintain adequate BP & HR. There initially is an immediate response with an abrupt fall in systolic and diastolic BP blood pressure and a rise in HR (first 30 s), with a phase of early stabilization, after 1-2 min, followed by a response to standing for more than 5 min. The normal response includes a rise in HR by 10-15 bpm and a slight decrease in systolic BP blood pressure, and in some a rise in diastolic BP by 10 mmHg is normal.[8 9] A systolic BP fall of more than 20 mmHg or more than 10 mmHg for diastolic BP or a rise in HR of more than 30 bpm (or 40/min in 12-19 yr olds) is considered abnormal.[5-9]

Another test measures changes in BP & HR during and after passive head-up tilting to 60 degrees on a motorised table.[10 11] The acute fluctuations seen in the active stand-up test are not observed in this test, and it is a predominantly neuro-cardiovascular autonomic response without the influence of the pumping action of leg muscles. To ascertain the responses to food and physical exertion when upright, the head-up tilt test is combined with a relevant provocative stimulus such as a balanced liquid meal or a modified exercise test.[5 7]

A variety of factors in daily life can influence neuro-cardiovascular autonomic responses, that including body position, emotional state, activity (physical or mental), food ingestion, medication for specific autonomic conditions[12] and associated disorders, and other non-prescribed substances. The COVID-19 pandemic emphasised the need to develop home-based testing, as assessments of even core stimuli, such as postural change, food ingestion and physical exertion were needed with

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inaccessibility in most of the specialised autonomic testing. The key aim was to enable the subject to conduct relevant tests themselves and report back to the clinician with their findings. This additionally enabled the individual and health care professional to understand the stimuli in daily life dependent on preserved autonomic function and evaluate factors that cause fluctuating symptoms. This is particularly relevant to Long Covid, which is characterised by a daily and weekly fluctuation of symptoms.

## Aims

To describe the adapted Autonomic Profile (aAP) test, provide a case example and discuss its role in evaluating and understanding neuro-cardiovascular autonomic dysfunction, and its role in aiding self-management in Long Covid and other conditions that cause autonomic impairment.

## Methods

The aAP protocol was initially developed by one of the authors (CJM) in the early phase of the pandemic to test patients remotely and avoid laboratory testing and travel to the hospital. It was based on experience over three decades and on information in the two autonomic departments that he developed and directed (at St Mary Hospital/Imperial College London and the Autonomic Unit at Queen Square, University College London). Pre-pandemic evaluation had utilised ambulatory and programmed BP/HR recorders (as used in hypertension assessment), with additional measurements while lying and standing, and to food and physical exertion.[13] [14] This became challenging during the pandemic as the equipment needed travel for collection and briefing, with uncertainty about sterilising recorders without damage to them, and to avoid them possibly transmitting the virus. The autonomic protocol was devised to overcome these issues and was further refined by authors MS and JC for particular use in Long Covid patients. It has gone through several iterative cycles of development using feedback from physicians, therapists, researchers and especially patients who now utilise the aAP to aid diagnosis and management.

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## The aAP protocol

The test involves measuring BP and HR at times as outlined below while at home, with a personal arm cuff (and not wrist) BP/HR monitor as recommended by the British Heart Foundation (giftshop.bhf.org.uk), whose website lists validated model. An example is Omron, also approved by the British Hypertension Society. The recordings provide information on neuro-cardiovascular autonomic responses to key activities in daily life such as postural change, and before and after food and exertion. Experience over the decades indicates that this protocol, even before the pandemic, provided adequate data to exclude autonomic dysfunction and initial autonomic diagnosis and guidance on treatment. The advantage with the aAP is that it can be repeated on a 'typical' or 'atypical' day and objectively can assess the response to intervention, be it non-pharmacological or pharmacological.

Unlike other standardised tests, there is no need to abstain from caffeine, nicotine, alcohol or medications for this test, as the purpose is to test in their daily life the reaction to common stimuli and record normal (or abnormal) autonomic responses to these stimuli.

To complete the aAP, time, position, BP, HR, and key symptoms in brief (such as dizziness), are recorded on the accompanying **aAP diary sheet**. This is of particular importance in autonomic conditions and differs substantially from BP/HR recordings commonly used for hypertension. Recordings should be taken on waking, after meals, after exertion and before sleep, with measurements taken as outlined below:

- **Waking** - The BP/HR is recorded after lying down, then after 3 minutes of sitting, and then after 3 minutes of standing.
- **Food/liquid intake** – Recordings 3-5 min after food ingestion at main meals (breakfast, lunch or dinner), lying down first, and then after 3 minutes of standing. A note is made of food and drink consumed (including alcohol).
- **Activity** – BP/HR recordings 3-5 mins after any activity (physical, cognitive or emotional) morning and afternoon, separated from meals **Physical activity** will individually differ and can be 5 minutes of walking, or going up and down a flight of stairs. **Emotional activity** might be watching an exciting sporting match or film. **Cognitive activity** might be 5 minutes working out a crossword puzzle. The subject should include at least one form of physical exertion if possible. Discussion with the clinical team will help determine the form of exercise or exertion that may be most appropriate.

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In those more severely incapacitated and disabled they can substitute sitting for standing, especially if after exertion or food. If the patient wishes to add Any additional activities, which cause or worsen symptoms, can be recorded with time, event/activity and position (lying, sitting, standing).

**Box 1. The aAP diary sheet**

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## The aAP diary sheet

**Name/ number:**

***Diet** – please state what food or drink, including alcohol, was consumed
***Activity/ exertion** (can be physical, cognitive or emotional) – please state what was the activity and for how long

| Enter time | Position/Activity | Blood Pressure | Heart Rate | Symptoms | Other details |
|---|---|---|---|---|---|
| **EARLY MORNING (ON WAKING)** Time: _ _ hr _ _min | | | | | |
| _ _ hr _ _ min | Lying | _ _ _/ _ _ _ sys. diast | | | |
| _ _ hr _ _min | After 3 min sitting | | | | |
| _ _ hr _ _min | After 3 min standing | | | | |
| **BREAKFAST** Time: _ _ hr _ _min; Details of diet*: | | | | | |
| _ _ hr _ _ min | Lying | | | | |
| _ _ hr _ _ min | After 3 min standing | | | | |
| **ACTIVITY/ EXERTION** Time: _ _ hr _ _min; Details of activity/exertion*: | | | | | |
| _ _ hr _ _ min | Before exertion | | | | |
| _ _ hr _ _ min | After 3 min exertion | | | | |
| **LUNCH** Time: _ _ hr _ _min; Details of diet*: | | | | | |
| _ _ hr _ _ min | Lying | | | | |
| _ _ hr _ _ min | After 3 min standing | | | | |
| **ACTIVITY/ EXERTION** Time: _ _ hr _ _min; Details of activity/exertion*: | | | | | |
| _ _ hr _ _ min | Before exertion | | | | |
| _ _ hr _ _ min | After 3 min exertion | | | | |
| **DINNER** Time: _ _ hr _ _min; Details of diet*: | | | | | |
| _ _ hr _ _ min | Lying | | | | |
| _ _ hr _ _ min | After 3 min standing | | | | |

| | | | | | |
|---|---|---|---|---|---|
| **BEFORE SLEEPING (IN BED)** Time: _ _ hr _ _min | | | | | |
| 22.15pm **(In bed)** | Lying in usual sleeping position (as with pillows) | | | | |

**Measure sitting BP/HR only if you find it difficult to stand.**

**Please record any other type of activity that you would like to tell us about and is not listed above, with time & position.**

| Enter time | Position/Activity | Blood Pressure | Heart Rate | Symptoms | Other details |
|---|---|---|---|---|---|
| _ _ hr _ _ min | | | | | |
| _ _ hr _ _ min | | | | | |
| _ _ hr _ _ min | | | | | |

The patient ideally needs to choose a day when they can complete all the measurements. The intent is to provide relevant autonomic information during a standard day with usual activities so that no change in

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schedule is needed. The aAP can be repeated on another day if needed for comparison after adjusting for the triggers and assessing the effectiveness of any interventions.

The subject will need to be still while BP & HR is recorded. As some may feel dizzy or possibly faint especially when standing, they ideally should lean against a wall or even have another person present whilst performing the test when standing. They should abandon the recording and sit or lie down if symptoms get worse.

**Box 2. Case example**

A 51-year-old school teacher tested positive for COVID in September 2020. Her acute symptoms resolved but after 6 months she had ongoing breathlessness, fatigue, palpitations, dizziness, and a feeling of "butterflies" in the stomach. 24-hour ambulatory ECG which demonstrated sinus tachycardia with a maximal HR of 154bpm.

She returned to work in April 2021 but with workplace modifications. Soon after her return she noticed worsening of symptoms on standing including dizziness and palpitations. Her smartwatch captured significant tachycardia episodes and also bradycardia episodes 148 and 35 respectively. Tilt table testing with 40-minute passive head up tilt in Jan 2022 on the advice of a cardiologist was inconclusive with no cause identified to explain her symptoms.

She completed an aAP in Feb 2022 which did not show significant BP changes but with certain stimuli, as indicated below, HR rose substantially fulfilling the criteria for PoTS on two occasions.

- *On walking, HR increased by 28 bpm after 3 min standing (when she was dizzy) with no significant change in BP*
- *After lunch (ham sandwich and diet coke), HR increased by 27 bpm after 3 min standing (headache) with no significant change in BP*
- *After mild physical exertion (putting away washed clothes, up and down the stairs twice), HR increased by 34 bpm after 3 min of standing (after exertion) and she was symptomatic with no significant change in BP*
- *After dinner (slice of toast, banana, decaf tea), HR increased by 40 beats/min after 3 min standing and became symptomatic (breathless) with no significant change in BP*

The aAP in this case was more sensitive for capturing evidence of dysautonomia through postural HR changes than would have been with a tilt table test. It also indicated a specific triggers one of which, food ingestion she was not aware of. She was advised on post-prandial triggers, and this included eating smaller portions if needed more frequently and reducing refined carbohydrates by switching to low glycaemic index foods.

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# Discussion

The adapted BP/HR autonomic profile is of value in the evaluation of neuro-cardiovascular autonomic dysfunction. It determines the response to various stimuli in daily life, such as postural change, food ingestion, physical activity and other activities (cognitive and emotive) that can affect such individuals. It determines if orthostatic hypotension, a marker of relatively rare conditions causing autonomic damage and failure (Table 1) is present, or can be excluded. It can confirm autonomic dysfunction in Long Covid and PoTS. It helps both the healthcare professional and the individual confirm which stimuli trigger autonomic dysfunction and provides a basis for rational management. Depending on the BP and HR responses this could include adjusting the amount of food intake and limiting or changing physical exertion, which are additional stimuli that can initiate or amplify autonomic dysfunction. Importantly this can be performed in a home setting independently by the subject, and repeated when needed or if there are lifestyle or medication changes, with positive and practical interaction with the healthcare professional. This avoids the dependence on evaluation in a controlled environment, such as an autonomic laboratory. The latter is important at times for diagnosis but has limitations in the number who can be assessed and its relevance to the individual in daily life.

The aAP thresholds to confirm orthostatic hypotension and postural tachycardia (as in PoTS) remain as previously established, with the former a common finding in autonomic damage/failure and the latter in conditions where there may be no apparent structural damage, such as in Long Covid and PoTS. In Long Covid it appears commonly and with fluctuant symptoms, which often are related to specific stimuli in daily life. The aAP provides both subjective and objective evaluation of the physiological and symptom variation with common stimuli. This approach also may explain Post-Exertion Malaise (PEM) or Post-Exertional Symptom Exacerbation (PESE), both described in Long Covid which can be triggered by various activities (physical, cognitive or emotional). It may be as proposed, that the immunological responses to exertion in Long Covid can worsen AD and contribute to relapse.[3]

In summary, given the large number with Long Covid (> 2 million in the UK alone) and that autonomic dysfunction needs evaluating, the BP & HR aAP is a practical means of autonomic

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assessment and also determining the impact of intervention in such individuals. This test can be further evaluated in large-scale Long Covid studies such as NIHR-funded LOCOMOTION.[15]

### Using the aAP protocol

The aAP self-report paper version is free to use, and the MS Word/ PDF copy is available on the ACNR website or University of Leeds website.

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