



# **The Effect of Exercise on Cold-Induced Neurovegetative Dysautonomia Blindness**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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**Case Study**

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## **ABSTRACT**

The autonomic nervous system (ANS) is responsible for regulating heart rate and blood pressure and maintaining homeostasis during physiological stresses. Nervous dysautonomias are often observed in patients presenting cardiovascular symptoms. Despite that, other important but less known conditions can be encountered. We report the case of a 19-year-old young man who presented for blindness occurring in the cold and improving with exercise. Investigations revealed neurovegetative dysautonomia with significant vagal hyperactivity associated with central B-sympathetic hyperactivity. Our patient received treatment based on hygienic and dietary measures with a combination of an anti-hypotensive drug such as Etilefrine. 2 months later, a re-evaluation showed a clear improvement, confirmed during the control neurovegetative exploration but also during the ophthalmological examination.

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## 1. INTRODUCTION

The autonomic nervous system (ANS) is responsible for regulating heart rate and blood pressure and maintaining homeostasis during physiological stresses. Nervous dysautonomias are often observed in patients presenting cardiovascular symptoms. In addition to the most common, high blood pressure, other important but less known conditions can be encountered. Our case presented in this article is a typical example of the rare manifestations revealing neurovegetative dysautonomia.

## 2. CASE PRESENTATION

Mr. Y.H. a 19-year-old young man without cardiovascular risk factors, has had monophthalmus of the left eye since birth. The patient presented to our ANS exploration unit for blindness occurring in the cold and improving with exercise, evolving for 5 months before his consultation without other symptoms, specifically no tinnitus or orthostatic dizziness, bloating in the abdomen, dysuria, or sleep disorders. Ophthalmological exploration found a drop in visual acuity rated 7/10, while the anterior segment, electroretinography, and fundus examinations did not reveal any abnormalities. The patient also received a neurological examination without abnormalities, and a brain MRI returned normal. Furthermore, a basic cardiovascular examination coupled with a transthoracic ultrasound was also without abnormalities.

Given the clinical orientation, in particular the improvement of symptoms during exercise, neurovegetative dysautonomia was suspected. We conducted a clinical exploration of ANS, carrying out several tests.

At rest, our patient had a minimum heart rate (HR) of 48 beats per minute (bpm) and a

maximum rate of 60 bpm (Fig. 1), with a systolic blood pressure (SBP) of 120 mmHg.

During the deep breathing test, we noted a 33% vagal response (HR max at 100 bpm; decrease in SBP from 120 to 106 mmHg). The hand grip test demonstrated a vagal response identical to that of the previous test, while the sympathetic response did not exceed 24% (Fig. 2).

The third test consisted of hyperventilation, during which the rate increased from 74 bpm to 94 bpm with a drop in SBP from 120 mmHg to 94 mmHg (Fig. 3).

As for the mental stress test, the B-sympathetic response was frankly high, with a percentage reaching 39%; however, the  $\alpha$ -sympathetic response was limited to 12%.

We finished our exploration of ANS with the orthostatic test, which also revealed a very significant vagal response, reaching 60% (Fig. 4).

At the end of our exploration, we concluded that there was significant vagal hyperactivity associated with central B-sympathetic hyperactivity, which could be consistent with the clinical presentation that our patient presented.

A treatment based mainly on hygienic and dietary measures was initiated: avoidance of triggering factors, wearing compression stockings, and rehydration (>1.5 l/d), a high salt diet (>6 g of sodium/d), and also the combination of an anti-hypotensive such as Etilefrine.

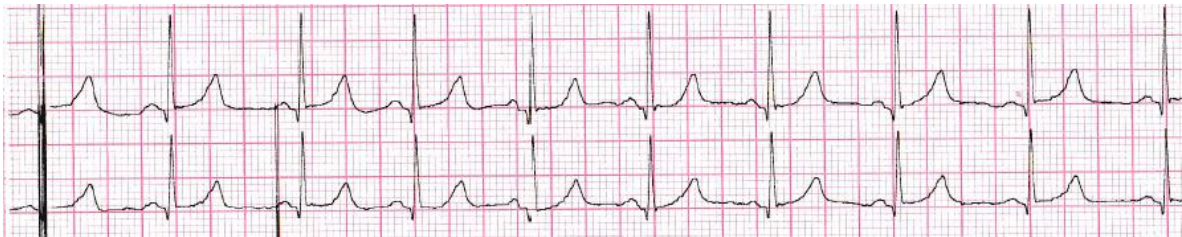
A re-evaluation was carried out after 2 months, showing a clear improvement, confirmed during the control exploration but also during the ophthalmological examination (Figs. 5-7).



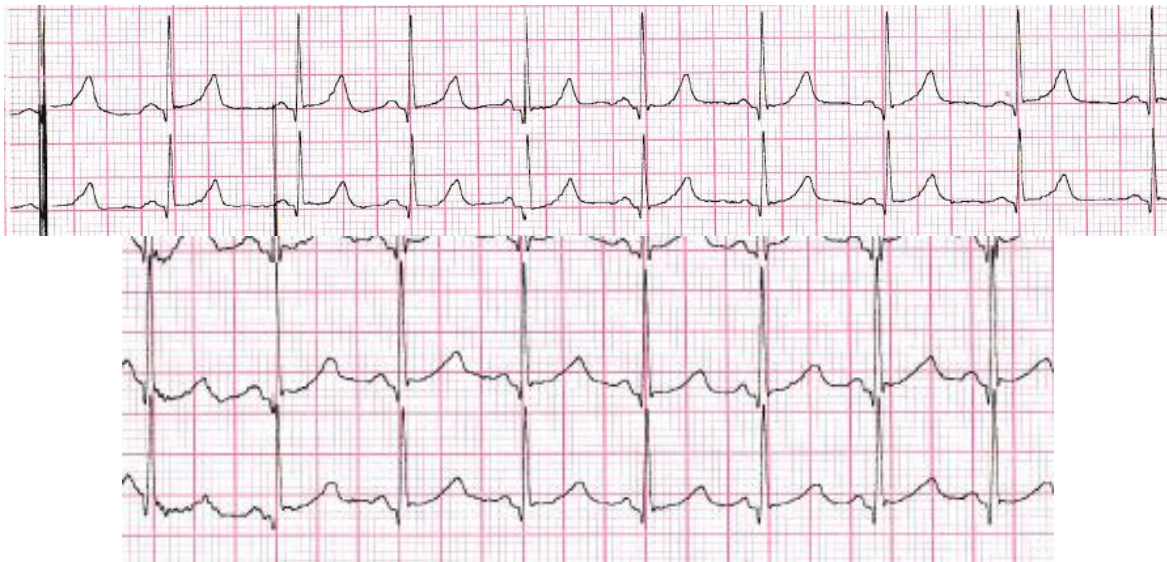
**Fig. 1. Resting ECG**



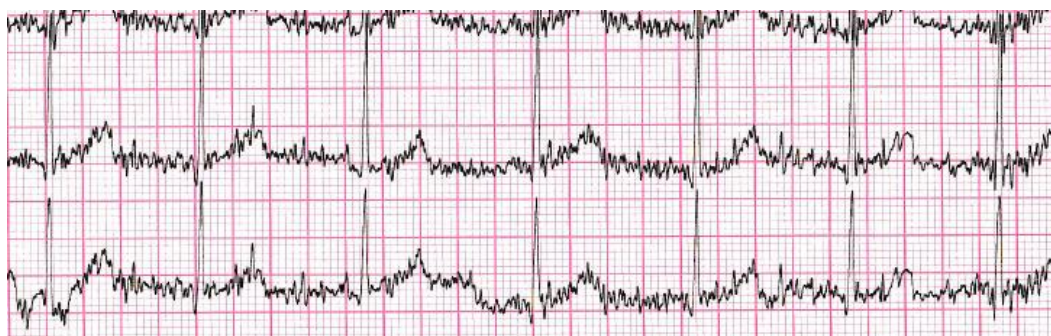
**Fig. 2. Hand grip test ECG**



**Fig. 3. Hyperventilation test ECG**



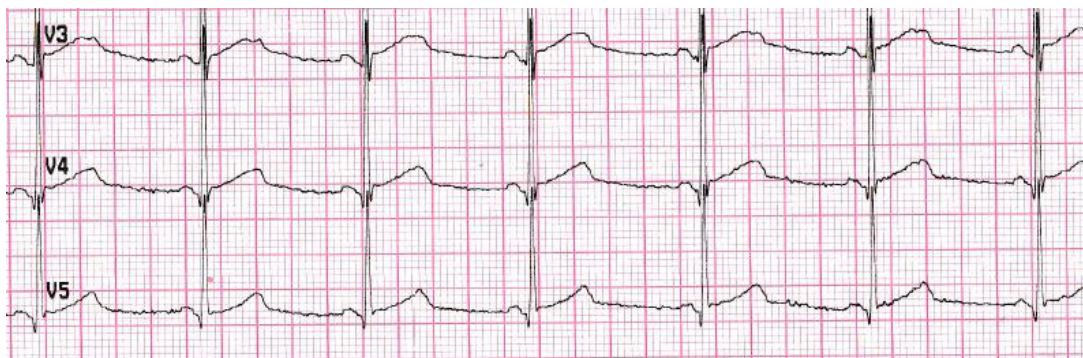
**Fig. 4. Orthostatic test ECG**



**Fig. 5. Hand grip test, control ECG**



**Fig. 6. Hyperventilation test, control ECG**



**Fig. 7. Orthostatic test, control ECG**

### 3. DISCUSSION

The autonomic nervous system (ANS) is made up of sympathetic, parasympathetic, and enteric components. The cardiovascular branch of the ANS is responsible for regulating heart rate and blood pressure and maintaining homeostasis during physiological stresses, including exercise and standing. The two crucial elements controlled by the ANS are the heart and the vessels [1–3].

Generally, autonomic dysfunctions are of multifactorial origin, accompanying diseases with central or peripheral involvement of the ANS and/or treatment with neurotoxic or cardiotoxic drugs. As a primary disease, it can be found in rare cases of primary autonomic failure. The disruption of autonomic nervous regulation in any reflex chain manifests itself in the corresponding organic system [4].

Autonomic symptoms can be divided into orthostatic, non-orthostatic, and diffuse. Orthostatic symptoms are generally associated with cerebral hypoperfusion. Common non-orthostatic symptoms include constipation,

bladder problems, intolerance to cold or heat, excessive sweating or loss of sweat, and erectile dysfunction. Common complaints also include fatigue, headaches, and insomnia [2].

In order to study the neurovegetative response during exercise and cold, several studies are carried out. Takuro Washio et al. studied the cerebral blood flow (CBF) in the posterior circulation and the anterior circulation during a cold pressor test (CPT). They revealed that the blood velocities and the dynamic cerebral autoregulation (dCA) of both circulations were unchanged at CPT. These findings suggest that CPT-induced elevations in arterial blood pressure and sympathetic nervous activity did not cause changes in CBF regulation in the posterior circulation compared with the anterior circulation [5].

In a study conducted by Billie K. Alba et al., an assessment of skin microvascular function was completed prior to and following the exercise intervention, and skin temperature and cutaneous vascular conductance data were collected during the acute exercise. It showed increased sympathetic cutaneous

vasoconstriction throughout the exercise in the cold via reduced skin temperature and a blunted increase in cutaneous vascular conductance, likely a response to limit heat loss in the cold environment [6].

The process of cardiac dysautonomia can be paroxysmal or chronic. Disorders of the sympathetic or parasympathetic systems can result in one action without opposition from the other. The most common cardiac manifestations of dysautonomia include reflex syncope, inappropriate sinus tachycardia, and orthostatic intolerance syndromes: orthostatic hypotension and postural orthostatic tachycardia syndrome [1].

Clinically, parasympathetic function is tested by measuring changes in heart rate in response to deep breathing, the Valsalva maneuver, and active standing. Sympathetic function is typically tested by measuring changes in blood pressure in response to the Valsalva maneuver, tilt table test, and active standing [7].

There are many additional tests of autonomic function that occur in other organ systems, such as urodynamic testing in urology, gastric emptying studies in gastroenterology, and pupillometry in ophthalmology [7].

The rare clinical presentation of our patient with a drop in visual acuity occurring during cold weather may be linked to orthostatic dysautonomia secondary to cerebral hypoperfusion. More likely an orthostatic cerebral hypoperfusion syndrome (OCHOs) without orthostatic hypotension, bradycardia, hypocapnia, and excessive tachycardia [2].

OCHOs was hypothesized to be caused by immune-mediated arteriolar dysfunction and cerebral autoregulatory failure as a result of abnormal cerebral arteriolar vasoconstriction. Thus, the OCHOs may have an immune-mediated basis and, theoretically, may respond to immunotherapy with IVIG while its effect is unclear [8].

OCHOs affects wide range of age groups and more women than men were affected. However, this could be due referral bias and needs to be confirmed in subsequent studies [9].

As a combined, hypertension and migraines account for 35% of OCHOs patients, making them the two most common comorbidities. SVD,

or small vessel disease, has been associated to both disorders [9–11].

In general, the therapeutic approach to orthostatic cerebral hypoperfusion syndrome is the use of calcium channel blockers or angiotensin-converting enzyme inhibitors for patients suffering from hypertension; and volume expansion with salt, fluids, Fludrocortisone, or the use of vasopressor medications in patients with hypotension [2].

In a cohort of young, healthy individuals, G.D. Miller et al. showed that exercise training in a cold environment can enhance dynamic cerebral autoregulation (dCA). The study also confirmed that these changes were not directly explained by a greater cerebral blood flow velocity or hemodynamics during acute exercise, nor were functional changes observed in peripheral vascular beds in the cold, and they concluded that exercise training in the cold may be a useful strategy to alter dCA [12].

The progression of autonomic dysfunction is associated with increased cardiovascular risk. Thus, regular screening and management of the risks of progression of neurovegetative dysautonomia are necessary. Clinical exploration of ANS is recommended once every two years. However, additional studies are needed to clarify the precise mechanisms underlying the association between the progression of autonomic dysautonomia and cardiovascular diseases [13].

Cardiologists are not always aware of cardiac dysautonomia because they typically focus on primary cardiac disorders such as heart failure, coronary artery disease, arrhythmias, and hypertension. However, being alert to the possibility of cardiac dysautonomia is very important, especially when dealing with patients with unusual symptoms and apparently normal vital parameters and ECGs.

#### 4. CONCLUSION

Besides the most common arterial hypertension, conditions such as postural orthostatic tachycardia syndrome, orthostatic hypotension, reflex syncope, and chronotropic insufficiency should be known by cardiologists. Cardiac dysautonomias vary in prevalence across the lifespan and may overlap, thus posing a challenge for a clinician. It is therefore important to recognize their manifestations,

the diagnostic methods, and the prognostic and therapeutic consequences.

## CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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