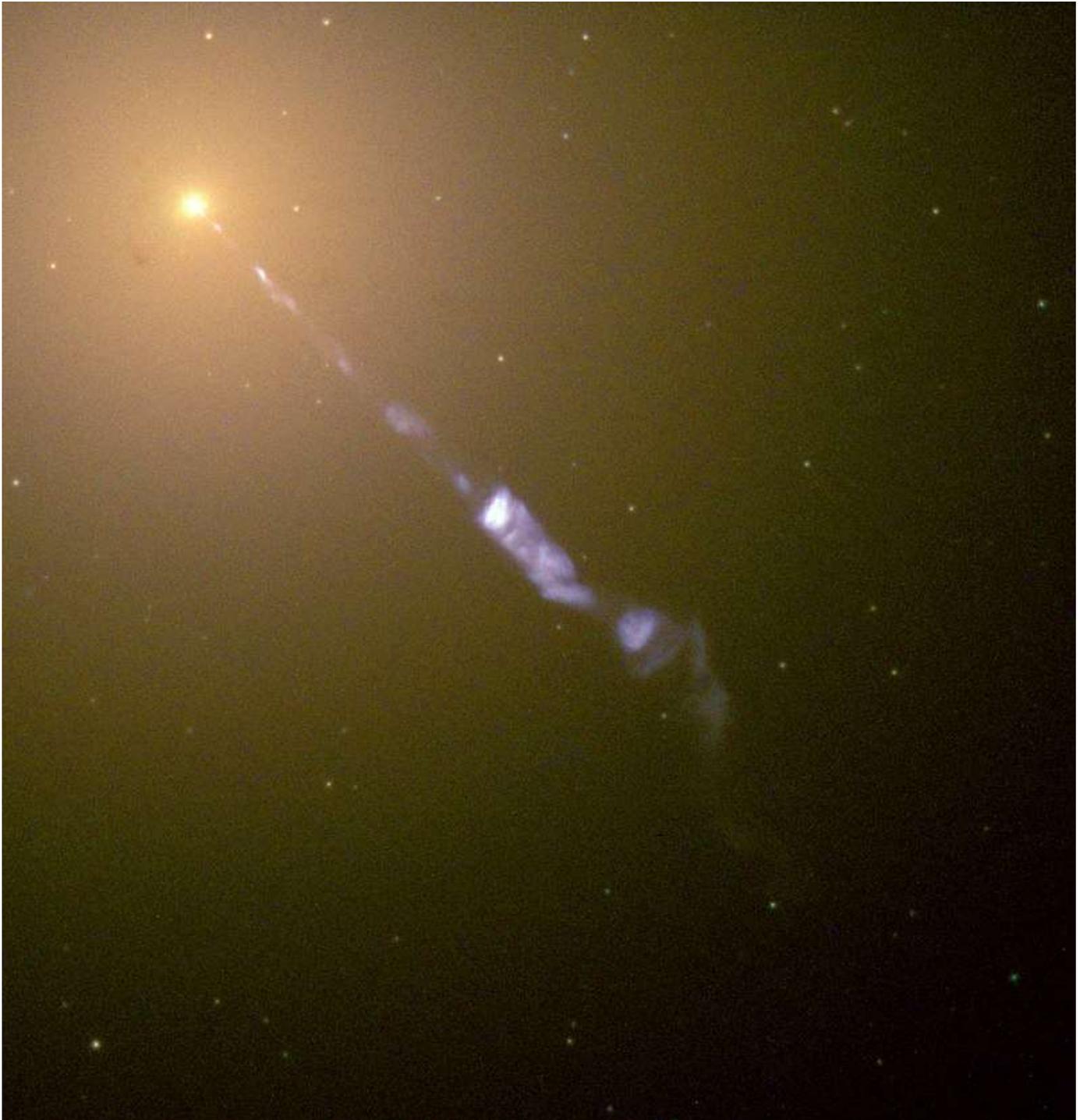


**CAROTID SINUS HYPERSENSITIVITY**



*Messier 87, (M87) (NGC 4486); elliptical galaxy with relativistic jet of 5000 light years. in the Constellation of Virgo, distance, 55 million light years, (Hubble Space Telescope).*

*“87: Nebula without star. This nebular appears of the same brightness as the two nebulae No’s 84 & 86”*

*Charles Messier, 18th March 1781.*

*“Very bright, pretty large, round and much brighter in the middle where there is a distinct nucleus....”*

*John Herschel (1792 - 1871)*

*“Exceedingly bright; No spiral structure is discernable. A curious straight ray lies in a gap in the nebulosity in PA 20°, apparently connected with the nucleus by a thin line of matter. The ray is brightest at its nearest end, which is 11" from the nucleus....”*

*Heber Curtis, 1918*

*On the night of the 18th of March, 1781, the famous French Astronomer, Charles Messier, discovered his 87th “nebula”. He was compiling a catalogue of “nebulous” objects, not because he was interested in them, but rather because he was **not** interested in them! What Astronomers at this time were intensely interested in, was comets, but in their scrutiny of the heavens they occasionally came across glowing objects which at first glance could be mistaken for a comet. However they were not comets as they remained fixed in the heavens in contrast to comets which streaked across them. What these nebulosities were nobody knew, nor much cared about, however they were most annoying objects as they distracted Astronomers from finding true comets. Accordingly Messier had decided to catalogue the positions of these nebulae, so that Astronomers would then know their locations and so be able to dismiss them and not waste time following them night after night.*

*By the Nineteenth century, telescopes had become more powerful and Astronomers became more interested in the mysterious nebulae now that they could discern them more clearly. John Herschel noted that M87 was not simply an amorphous glowing light, but that it actually had some complex structure. He had observed a distinct brighter central nucleus. With the advent of Astrophotography Heber Curtis in the early Nineteenth century made the first deep exposures of M87 to get a better look at it. What he found astonished him. It appeared that the object was emitting an immense “jet” of light from deep within its center that reached out for light years into space!*

*Advances in Astronomy were made at quantum leaps in the first decades of the Twentieth century. One of the most momentous was by Edwin Hubble who established that many “nebulae” were in fact other very distant “island Universes” that lay beyond our own galaxy the Milky Way. These “island Universes” turned out to be other Galaxies. What was truly staggering was the sheer number of them - seemingly there were as many if not more galaxies as there were stars in our own! The Universe had suddenly become a vast domain of dimensions beyond human undemanding. It turned out that not all nebulae were galaxies, some were star clusters (either open or globular) and some were simply immense amorphous clouds of gas and cosmic dust. In the case of Messier’s M87, this turned out to be a particular type of galaxy, known as an elliptical galaxy, (the others in*

*broad terms, being Spirals, of which the Milky Way is one example, Barred spirals, Lenticulars and Irregulars). But if M87 was a galaxy then it was a decidedly odd one with its mysterious, jet.*

*By the mid-Twentieth century "Radio"-Astronomers began to scan the heavens in wavelengths beyond normal visible light, including ultraviolet, infrared, microwave, and gamma waves. Suddenly a whole new Universe of astonishing images came into view. Wondrous new objects were discovered, and like the nebulae that so perplexed Eighteenth and Nineteenth century Astronomers, their natures were entirely unknown. One of the most perplexing were the Quasars, or "Quasi-stellar objects", discovered by Maarten Schmidt in 1963. They were not stars, but seemingly energy sources of very "small" (in cosmic terms) size - about the size of our own Solar System, but of immense, energy that produced a cosmic "jet" accelerated at relativistic speeds and that extended for thousands of light years. It was as if some cosmic sized alien was firing a "ray gun" out into the abyss of space. The Quasars were very distant, some at thirteen billion light years away were at the very edge of the observable Universe and in consequence incredibly ancient, born not long after the origin of the big bang itself. But Quasars were not the only strange new objects discovered by the new Radio-Telescopes.*

*In 1943 Carl Seyfert had discovered galaxies which seemed to radiate relativistic jets, similar to Quasars. These jets originated from deep within the center of the galaxy, and they became known as "Seyfert Galaxies". Like Quasars, the cause or source of the jet was unknown. Then galaxies were discovered that produced not one jet, but two, each radiating at 180 degrees from each other in the opposite direction. Again these jets seemed to be coming from the very center of the galaxy. As these jets were detected mainly in radio waves, these galaxies came to be known as Radio-Galaxies. Finally a fourth strange object was discovered, a single source of intense radiating energy, again not from any star, but this time there was no "jet" as such, rather just a glowing ball of immense energy, the brightest objects in the known Universe which became known as BL Lacertae Objects, or more simply. "Blazars".*

*If the Twentieth century proved to be the Renaissance of Astronomy, with rates of advancement not seen since the time of Galileo, then the early decades of the Twenty First century is the new Golden Age of Astronomy, unparalleled since the time of Claudius Ptolemy in the Second century A.D. It is the age of the Planet Hunters, of remarkable advances in the understanding of Astrophysics and of technological miracles that have transformed our undemanding of the Universe in ways that would have been inconceivable just a generation ago. It is now understood that at the center of (probably) all great galaxies lurk super-massive black holes of unimaginable forces, some containing as much mass as billions of Suns, concentrated into the size of a Solar system - or less - and driven by laws of physics completely unknown to us. Within a certain percentage of these - perhaps around 10% - great clouds of gas and cosmic dust come near the black hole attracted by its irresistible force of gravity - a force so powerful that not even electromagnetic radiation accelerated to the speed of light can escape from beyond its event horizon. As vast accretion discs form near them, matter is forged into a monstrous torus travelling at close to the speed of light - this creates heat of millions of degrees and by mechanisms not currently understood two "jets" are produced opposite each other that are accelerated outward at relativistic speeds for thousands of light*

years. Galaxies that have these accretion discs orbiting their central super-massive black holes may become "Active Galaxies". They have an "active galactic nucleus" or AGN. Twenty first century Astrophysicists now believe that when observed from the Earth four morphological types can be seen depending on their exact orientation with an observer on Earth. If very far distant, then the galaxy will be so dim as to be indiscernible - only its active galactic core is energetic enough to be detected. This is what Quasars are now believed to be. If the galaxy can be made out as well as one of its jets - this is a Seyfert galaxy. If the galaxy lies exactly horizontal to our line of sight we see both jets - this is a Radio galaxy. If the active galaxy's jet is aligned directly towards us, this is a Blazar. The mysterious objects that radio astronomers discovered in the Twentieth century are all manifestations of the same thing - active galactic nuclei - it's simply that we see them from different angles of orientation.

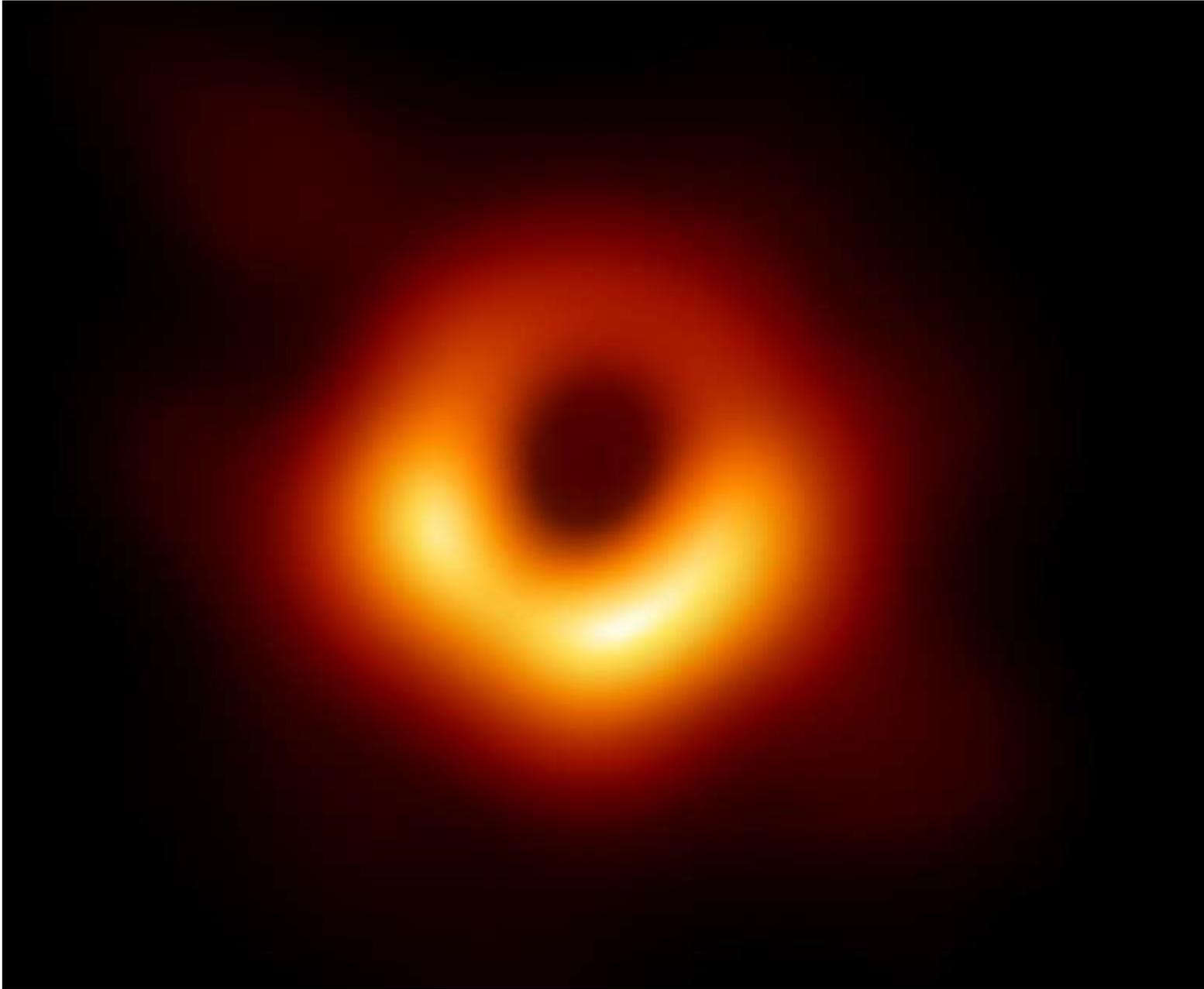
Our own Milky Way has a central super massive black hole - but it has no accretion disc surrounding it and so our galaxy does not have an active core (or nucleus) - most fortunately for anything in the path of the jet that this would produce. In the far distant future when the galaxy of Andromeda collides with the Milky Way, it is thought that the central black holes of the two will collide and merge, and from the gathering accretion disc of matter the new core will ignite relativistic jets. Some future intelligent civilization viewing this event from 13 billion light years away will see us then as a Quasar.

We live in the third Golden Age of Astronomy, (after the ages of Ptolemy and of Galileo). Twenty first century understanding of many aspects of the Universe would have dumbfounded Astronomers of the Eighteenth century. We live in a time of incredible new advances in our understanding of the cosmos. New discoveries are being made almost weekly. Until as recently as 1995 we had no idea if planets existed in other star systems, we now know of many thousands, and this is just the very beginning. But if one image will stand out from our time for centuries to come it will be the first ever image of a Black Hole, or at least the accretion disc surrounding one, as Black Holes themselves cannot be seen as no light can escape from within the event horizon that surrounds it. The image was created on April 10, 2019 by the global network of radio telescopes collectively known as the Event Horizon Telescope. It shows a superheated accretion disc of millions of degrees. The Black Hole's mass is estimated to be the equal of a staggering 6 billion Suns and its diameter a modest - in cosmic terms - 270 AU (i.e Sun - Earth distances). This black hole's accretion disc, as expected, produces a relativistic jet inclined at an angle of 17 degrees to the line of sight from the Earth. The Black Hole lies at the center of a super massive elliptical galaxy, 55 million light years from the Earth. Its designation is M87.

Charles Messier's unwanted nebulous object no. 87 today is seen as the one of the greatest wonders of the Universe. It is not a nebula in the modern sense. It is a galaxy and it is a galaxy that has an active galactic nucleus, and as such it produces two relativistic jets, one of which can be seen from the line of sight from the Earth.

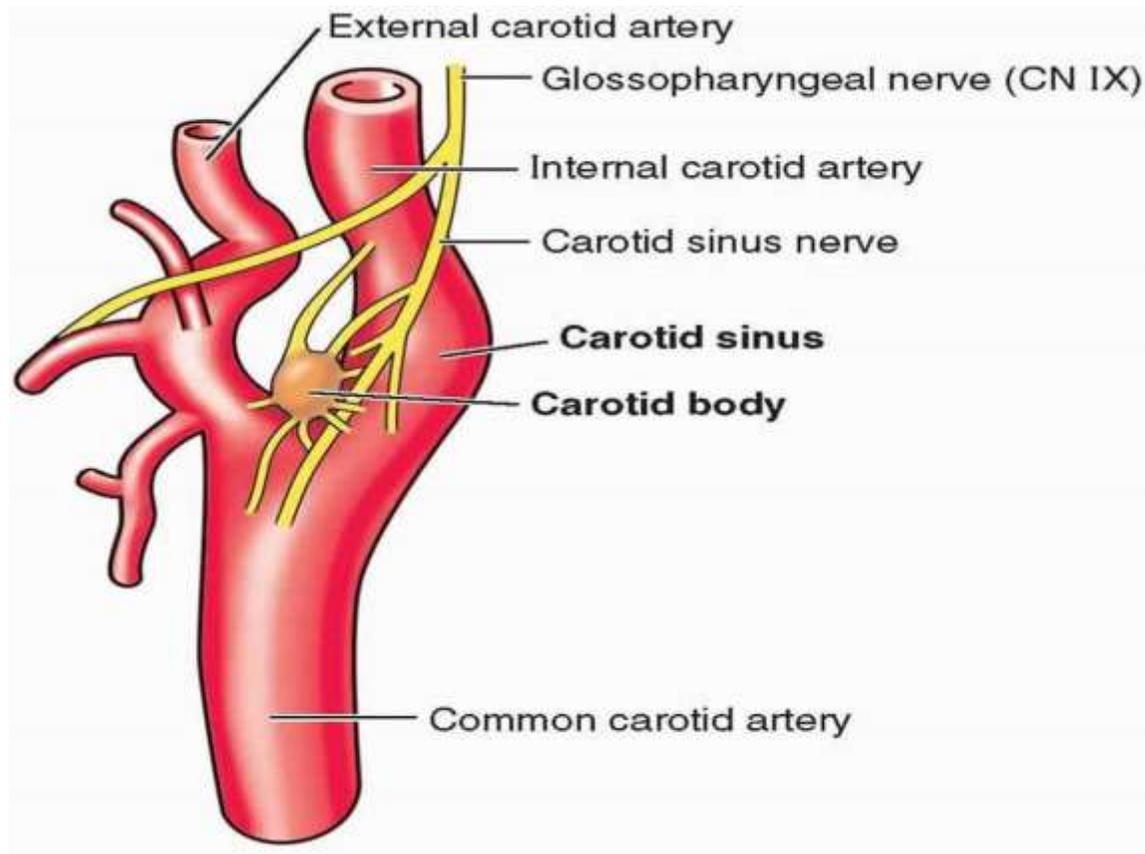
Just as in the field of Astronomy in the field of medicine we seek to find unifying truths that may explain a host of apparently disparate observations. There are many manifestations of syncope, among these are three of puzzling causation -

*Cardioinhibitory, Vasodepressor and Mixed. It now appears that, like active galactic nuclei, these are all simply different manifestations of single underlying entity.*



*The first photograph of a Black Hole. The event horizon of a super-massive black hole at the center of the monstrous elliptical galaxy, NGC 4486, better known as Messier Object, 87. Image in 1.3 mm infrared, Event Horizon Telescope, global network of radio telescopes, April, 2, 2019.*

## CAROTID SINUS HYPERSENSITIVITY



*The right common carotid artery bifurcation (medial view).*

### Introduction

**Carotid sinus hypersensitivity (CSH)** consists of the observation that stimulation of the carotid artery baroreceptors in the neck results in an exaggerated or *greater than expected*, fall in heart rate and / or in blood pressure.

The condition may result in pre-syncope, syncope, or unexplained falls, especially in the elderly.

**CSH** is a potent contributory factor and a potentially treatable cause of unexplained falls and syncopal episodes in **elderly people**. **Despite this the entity is often not considered.**

Carotid sinus *hypersensitivity* does not require treatment of itself, unless it is causing **symptoms**, resulting in carotid sinus *syndrome*.

## Terminology

**Carotid sinus hypersensitivity** is not of itself a clinical condition requiring treatment.

**Carotid sinus syndrome (CSS)** refers to the spontaneous **clinical manifestation** of **carotid sinus hypersensitivity** when changes in heart rate and/or blood pressure result in **symptoms**.

Carotid sinus syndrome is also sometimes referred to as **carotid sinus syncope**

## Epidemiology

**Carotid sinus hypersensitivity** is observed in up to 14 % of elderly nursing home patients and 30 % of elderly patients with *unexplained* syncope and drop attacks.<sup>1</sup>

**Carotid sinus hypersensitivity** is predominantly a disease of elderly people; it is virtually unknown in people < 50 years.

**Carotid sinus syndrome** is predominantly seen in males > 65 years of age, however it is also well documented in younger age groups as well.<sup>3</sup>

## Anatomy

The **carotid baroreceptors** are specialized tissues that are sensitive to mechanical pressure.

They are located bilaterally approximately with the **carotid sinuses** at the bifurcation of the common carotid artery into the internal and external carotid arteries.

The carotid sinus reflex plays a central role in blood pressure homeostasis.

Changes in stretch and transmural pressure are detected by baroreceptors in the heart, **carotid sinus**, aortic arch, and other large vessels.

Afferent impulses are transmitted by the carotid sinus, glossopharyngeal, and vagus nerves to the nuclei tractus solitarius and the para median nucleus in the brain stem. Efferent limbs are carried through sympathetic and vagus nerves to the heart and blood vessels, controlling heart rate and vasomotor tone.

A rise in blood pressure therefore results in enhanced vagal tone and inhibition of sympathetic tone, that results in bradycardia and peripheral vasodilation, which in turn results in a lowering of blood pressure, back to normal levels.

Note that the **carotid sinus** should not be confused with the **carotid bodies**, which are chemoreceptors, that respond to changes in arterial oxygen and carbon dioxide partial pressures.

## Pathophysiology

Although baroreceptor function usually diminishes with age, some people experience **hypersensitive** carotid baroreflexes. For these individuals, even mild stimulation to the neck results in marked bradycardia and/ or a drop in blood pressure.

The exact mechanism of this abnormal sensitivity is unknown.

In such people, carotid baroreceptor stimulation (e.g. such as may occur with turning of the neck or looking upward) results in *excessive* vagal activation and/or sympathetic inhibition, with a loss of cerebral perfusion that results in syncopal symptoms.

Carotid sinus hypersensitivity predominantly affects **older males** who have atherosclerotic vascular disease.

However, carotid sinus hypersensitivity may also be observed in individuals who have acquired abnormalities within the neck including:

- Prior neck surgery and/or irradiation therapy.
- Tumors in the region of the carotid sinuses.

## Classification

There are 3 *subtypes* of carotid sinus hypersensitivity described:

### 1. Cardioinhibitory, (around 70 % of cases):

- This is diagnosed if carotid sinus massage (CSM) results in  $\geq 3$  seconds of asystole

The predominant manifestation is a decreased heart rate, which results in sinus bradycardia, atrioventricular block, or asystole due to vagal action on sinus and atrioventricular nodes. The response can be abolished with **atropine**.

### 2. Vasodepressor i.e vasodilation, (around 10 % of cases):

- This is diagnosed if carotid sinus massage results in a fall in systolic blood pressure of  $\geq 50$  mm Hg

The predominant manifestation is a vasomotor tone decrease without a change in heart rate.

The significant resulting drop in blood pressure is due to a change in the balance of parasympathetic and sympathetic effects on peripheral blood vessels. This response is *not* abolished with atropine.

3. **Mixed, (around 20 % of cases):**

- This is diagnosed if *both* cardioinhibition and vasodepression are present.

Here both bradycardia and vascular dilation work synergistically to produce symptomatic hypotension.

### Clinical features

Patients may clearly relate symptoms to **neck movements** or **mechanical distortion**, however more often such a clear history is not obtained.

Carotid sinus *hypersensitivity* is a relatively common observation but it is only an *infrequent* cause of symptoms.

There is a lack of universal consensus, however in *general* terms, **carotid sinus hypersensitivity** is a *clinical observation* off **carotid sinus massage** that results in:

1. **Heart rate pauses**

- Duration of **> 3 seconds**

*However*, a pause as long as **6 - 9 seconds** may be necessary to overcome residual neural energy stores, and induce symptoms in some subjects.

Some Cardiologists, prefer a definition of **> 5 seconds**.

*And/or*

2. **A drop in systolic blood pressure**

- Of **> 50 mmHg**

**Carotid sinus hypersensitivity** is not of itself a clinical condition requiring treatment.

**Carotid sinus syndrome** refers to the spontaneous **clinical manifestation** of **carotid sinus hypersensitivity** when changes in heart rate and/or blood pressure result in **symptoms**.

Symptoms can include:

1. Pre-syncope
2. Syncope, (most commonly)
3. Unexplained falls, especially in the elderly.

### Carotid sinus massage:

**Carotid sinus hypersensitivity** can often be confirmed by careful **carotid sinus massage**, whilst the patient is on ECG monitoring and having blood pressures taken.

Monitoring is best achieved with a specialized beat-by-beat non-invasive HR/BP monitor device (e.g. Finapres).

### Contraindications:

Carotid sinus massage should be **avoided** in patients with:

- Prior transient ischemic attack or stroke within the past 3 months
- Carotid bruits (unless carotid Doppler studies have excluded significant stenosis)

### Technique:

- The patient is placed in the supine position with the neck extended (i.e, raising the chin away from the chest) to maximize access to the carotid artery.

The carotid sinus is usually located inferior to the angle of the mandible at the level of the thyroid cartilage near the arterial impulse

- Pressure is applied to one carotid sinus for 5 to 10 seconds.

Although pulsatile pressure via vigorous circular motion may be more effective, steady pressure is recommended because it may be more reproducible.

If the initial response is non-diagnostic, the procedure should be repeated on the contralateral side (unless contraindicated) following a one- to two-minute delay.

- Symptoms associated with CSH are rarely induced unless carotid sinus massage is carried out with the **patient in is the upright position**. This is most safely accomplished with the patient gently secured on a **tilt table** so the patient can be prevented from falling.

If the response is non-diagnostic in the supine position, the procedure should be repeated with the patient seated upright or positioned head-up on a tilt table

Testing is positive for CSS if the patients' **symptoms are reproduced** and other **causes of syncope have been excluded**.

### Differential diagnoses:

In regard to pathophysiology, **carotid sinus syncope** is similar, in terms of cardioinhibition and vasodilation components, to other forms of **reflex syncope** such as **vasovagal syncope**.

Precipitating factors, however, for these two types of reflex syncope differ.

Carotid sinus syncope is attributed to mechanical stress on hypersensitive carotid baroreceptors whereas vasovagal syncope is most often triggered by emotional events, painful stimuli, or prolonged upright posture.

Other reflex faints (e.g., **valsalva type syncopes**) may also need to be considered depending on the specific scenario of the patient's presentation.

### Investigations

There is no specific blood test or imaging study which confirms the diagnosis of Carotid sinus hypersensitivity / Carotid sinus syndrome.

Investigations therefore are done on order to exclude alternative diagnoses for pre-syncope/ near syncope.

A **12 lead ECG** is routinely done for any syncope patients presenting to the Emergency Department.

### Management

Patients with isolated carotid sinus *hypersensitivity* who remain **asymptomatic** require no specific therapy.

Patients with carotid sinus **syndrome** will require a **permanent cardiac pacemaker**.

In a minority of cases, the vaso-depressor (i.e **vasodilation**) - component of the reflex is particularly strong and so **vasoconstrictor drugs** may also be needed. **Midodrine** is one agent that is used in these situations.

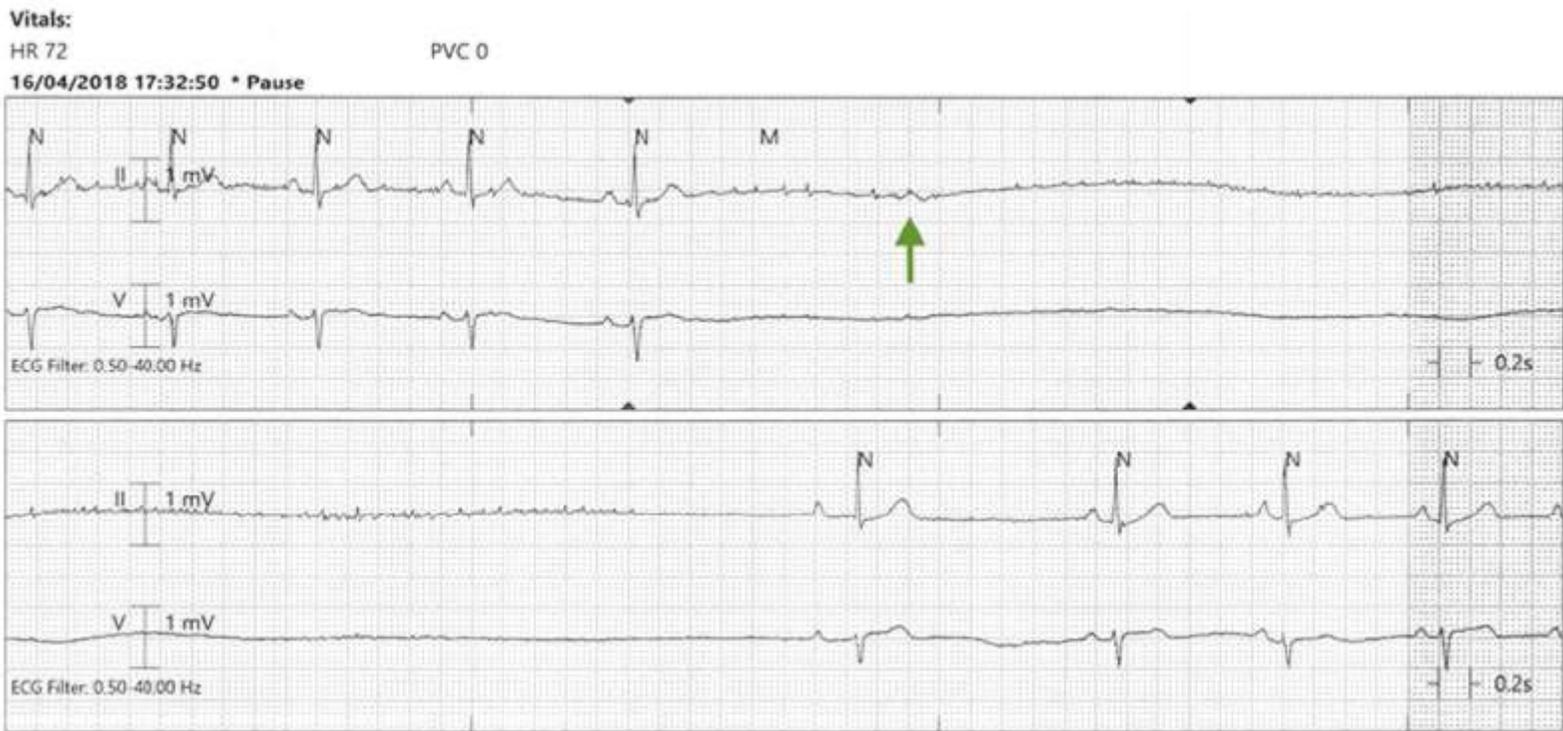
Restrictions should be placed on driving until appropriate treatment has been provided.

### Disposition:

Patients suspected of having **carotid sinus syndrome** should be referred to a specialist Electrophysiologist Cardiologist.

## Appendix 1

### Case report:



Vahid Moosavi et al. MJA

*A 55-year-old otherwise healthy woman presented with the first episode of syncope, preceded by sudden onset neck pain, while driving her car at low speed, leading to a minor car accident.*

*Clinical examinations, brain and neck magnetic resonance imaging scans and echocardiography were unremarkable.*

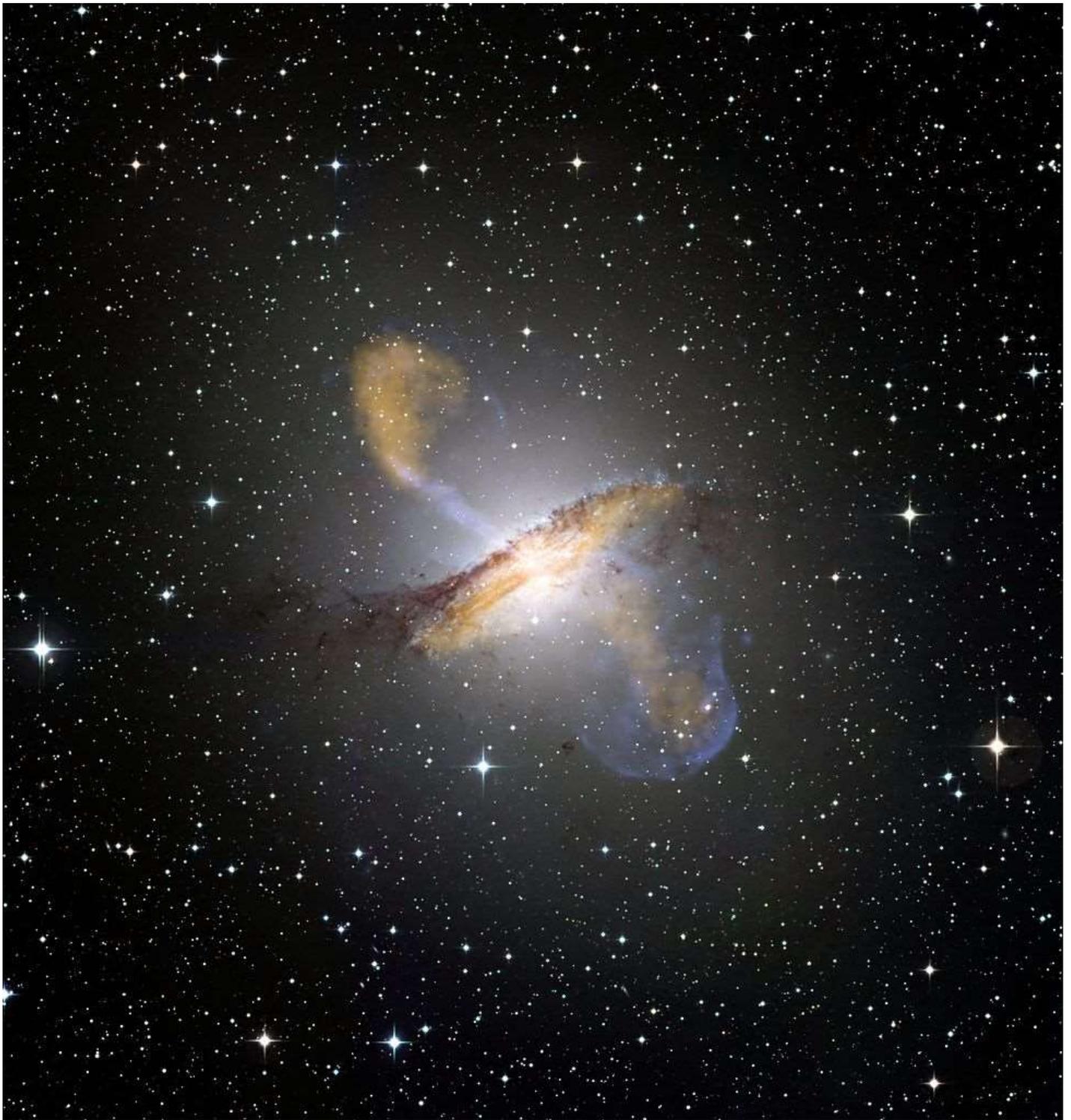
*Carotid sinus massage on the left carotid sinus induced the same syncopal symptoms associated with significant sinus pause.*

*The baseline electrocardiogram demonstrated normal sinus rhythm. A non-conducted P wave (green arrow) was noted soon after the carotid sinus massage followed by a prolonged episode of sinus arrest (10.4 seconds). This was consistent with high vagal tone resulting in transient sinoatrial and atrioventricular nodes block.*

*The sinoatrial node activity slowly resumed once carotid sinus massage was ceased.*

*She was diagnosed with carotid sinus hypersensitivity and underwent permanent pacemaker implantation.*

*Carotid sinus hypersensitivity is a rare condition usually seen in older men. This case, however, reminds us that carotid sinus hypersensitivity should be excluded when dealing with syncope of unknown aetiology even in younger patients.*



*NGC 5128, (or Centaurus A) - one of the most spectacular examples of a galaxy with an active galactic nucleus, in this case a Radio galaxy. Lobes and jets can be seen radiating from the galaxy's central super-massive black hole, distance, 15 million light years, (colour composite image, ESO, 2009).*

*This galaxy was discovered by the Scottish-Australian Astronomer, James Dunlop from his home in Parramatta, in New South Wales in 1826.*

*Centaurus A is a starburst galaxy, i.e a galaxy undergoing an exceptionally high rate of new star formation. This is thought to be as a consequence of its formation from the collision of a large elliptical galaxy and a smaller spiral galaxy. Merger of the two galaxies' central black holes probably resulted in the accumulation of an accretion disc, which ignited the jets, a fate that possibly awaits our own galaxy, when it collides with M31, (Andromeda) at some far distant point in the future.*

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Dr. J. Hayes  
1 August 2019.