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Review Article

Nerves of the heart: a comprehensive review with a clinical point of view

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ABSTRACT

The heart is an organ which main characteristic is its autonomy of function. Therefore, it is possible to develop elementary experiments such as extirpating the heart of a frog (*Bufo amenarum*), which during a certain amount of time keeps beating and even responding to brady- or tachycardian chemical stimulations. The underlying cause of this phenomenon is the action of specific solutions, which shower the mentioned organ. However, inside the organism, it adapts its functions to the somatic reality and to the specific moment of that soma. These conducts are instrumented by a complex system of information gathering, the adoption of central nervous system's function standards, and the production of functional responses suitable for the different possible situations. All these functions are related to cardiac innervation. © **Neuroanatomy. 2009; 8: 26–31.**

Key words [nerves of the heart] [anatomy of the ischemic pain] [clinical application of the anatomy]

Introduction

The consecutive cardiac cycles of contraction and relax on mammals have a myogenic origin. This is to say, it is generated in an autonomic form in the myocardium, independently from the organ innervation. The beginning and propagation of the potential of action is maintained by the conduction system. Therefore, the cardiac nerves would not be essential in the cardiac activity [1].

The heart receives the innervation of all the autonomic nervous system: the sympathetic trough the sympathetic chain; the parasympathetic through the vagus (pair X).

Sympathetic fibers

The preganglionic sympathetic fibers are located in the lateral column of the spinal cord. These fibers give origin to the three cervical ganglions and to the first three or four thoracic ganglions [2].

The cardiac branches of the superior ganglion or cardiac superior nerve (located in front of the CII and CIII vertebras) are originated on the inferior sector of the mentioned ganglion. There are existing branches that shunt it with the fillets originated in the other cervical ganglions. These cervical ganglions go down the primitive carotid and in front of the large muscle of the neck.

The middle cervical ganglion is tiny and can be absent (it is located on the same height than the CVI, near the inferior thyroid artery). Its cardiac branch, the middle cardiac nerve, arises independently or emerges after the shunt with the inferior cervical ganglion. On the right side, it descends behind the primitive carotid and keeps its way to constitute the dorsal part of the cardiac plexus (see forwards). In its way, it receives numerous boughs that come from the principal pneumogastric and the recurrent. On the left side, the nerve enters the thorax between the left primitive carotid and the subclavian, and it converges at the deep part of the cardiac plexus.

The inferior cervical ganglion is situated between the base of the transverse process of the last cervical vertebra and the neck of the first rib, on the medial side of the costocervical artery. Its cardiac branch, the inferior cardiac nerve, descends behind the subclavian artery (in this place it converges with the recurrent nerve and with a branch of the medium cervical nerve), and all along the anterior surface of the trachea, finally joining to the deep part of the cardiac plexus [2].

It also exists the possibility of a fourth cardiac nerve, which comes from the thoracic ganglion.

These branches, widely shunted in between, are grouped behind the aortic arch [3].

Parasympathetic fibers

The parasympathetic innervation arrives to the heart by means of branches of the pair X. The preganglionic vagal fibers flow from the brainstem, particularly from the bulbus (nucleus ambiguus, reticular nucleus and dorsal nucleus of vagus nerve). Traditionally, there are two types of fibers to describe, poorly differentiated:

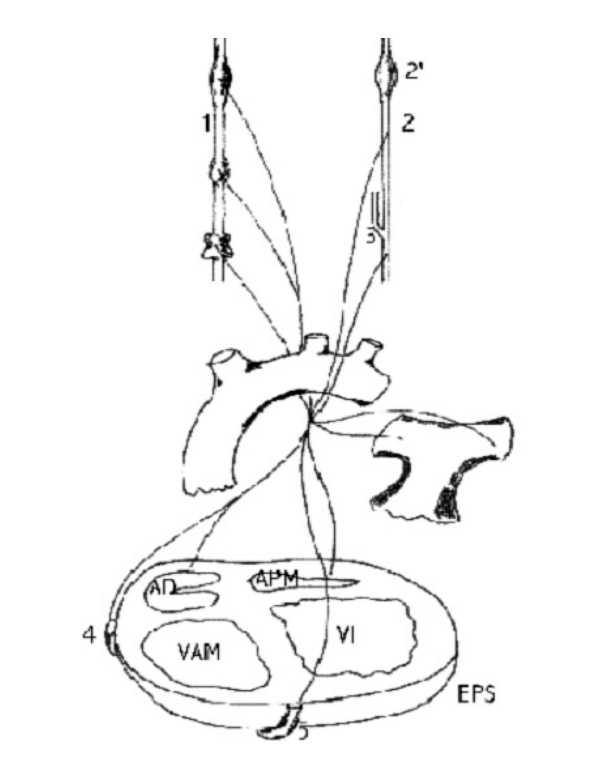

Figure 1. Schema showing the distribution of the sympathetic and parasympathetic branches that will become part of the cardiac plexus. Notice that the sympathetic branches go behind the aortic arch and the parasympathetic branches of the pair X will do it in the front. *(**1:** Sympathetic cervical chain; **2:** pair X; **2':** plexiform ganglion; **3:** inferior laryngeal nerve; **4:** right coronary plexus; **5:** left coronary plexus; **AD:** right atrium; **APM:** left atrial; **VAM:** right ventricle; **VI:** left ventricle)* (Illustrated by Eduardo Spinelli, MD)

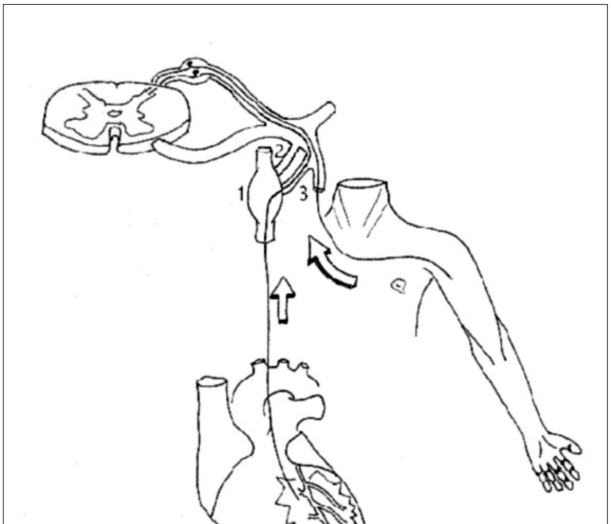

Figure 2. Schema where it is shown the cardiac efferent route, used for the perception of pain (for details please refer to the text). *(**1:** paravertebral sympathetic ganglion; **2:** grey rami communicans; **3:** white rami communicans)* (Illustrated by Eduardo Spinelli, MD)

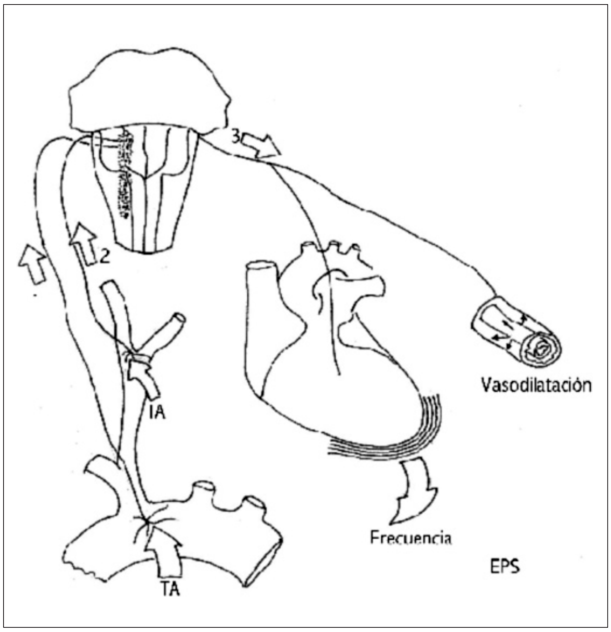

Figure 3. Scheme of blood pressure and heart rate regulation. *(**1 and 3:** pair X; **2:** pair IX; **IA:** glomus carotideus; **TA:** blood pressure; **Frecuencia:** heart rate)* (Illustrated by Eduardo Spinelli, MD)

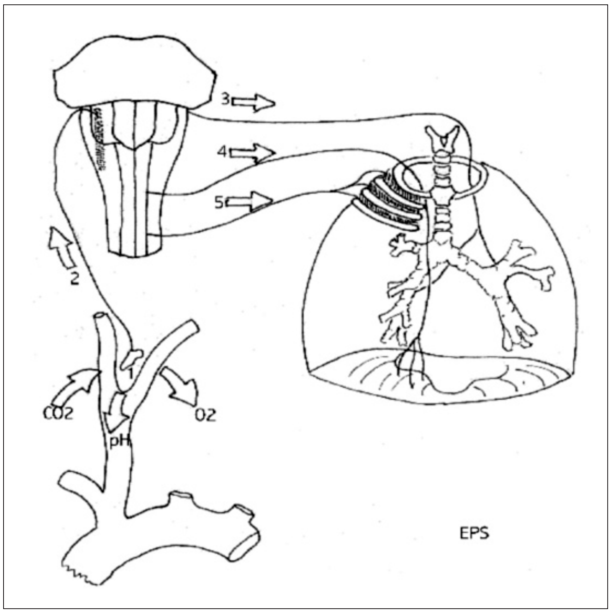

Figure 4. Scheme of the monitoring of the oxygen pressure through the cardiac plexus and its relationship with the function of the respiratory muscles. *(**1:** carotid body; **2:** pair IX; **3:** pair X; **4:** phrenic nerve; **5:** intercostal nerves)* (Ilustrated by Eduardo Spinelli, MD)

1. The superior cardiac nerves: from one up to three nerves are born in the origin of the superior and inferior laryngeals.

2. The inferior cardiac nerves: they are born under the origin of the recurrent. These fibers are grouped in front of the aortic arch and they become preganglionic fibers when they cross the little numerous ganglions that exist in the aorticopulmonary [4].

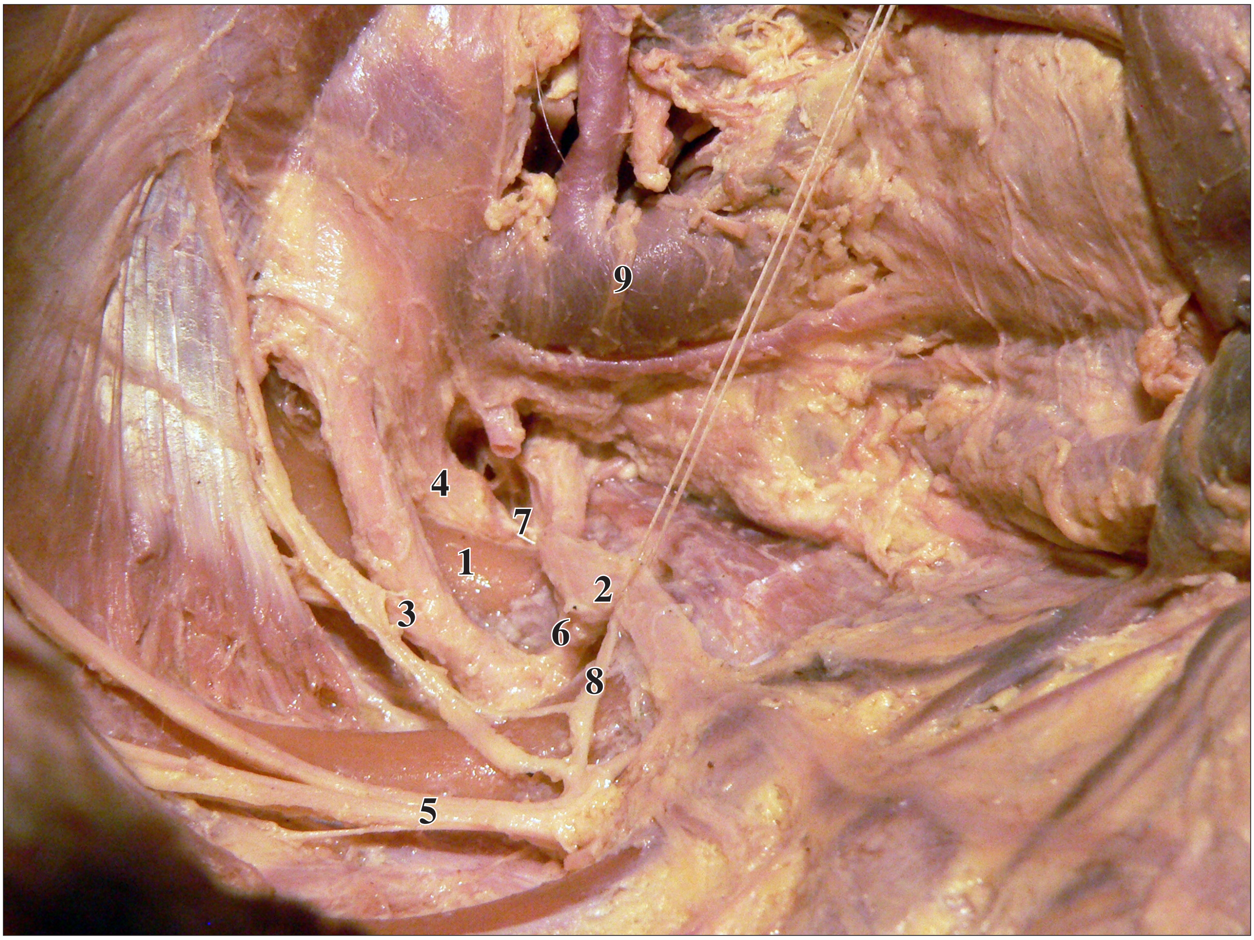

Figure 5. Pleural cavity. *(**1:** first rib; **2:** sympathetic nerve; **3:** first thoracic spinal nerve; **4:** 8th cervical spinal nerve; **5:** 1st intercostal nerve; **6-7:** rami communicans between sympathetic nerve and brachial plexus; **8:** rami communicans between sympathetic nerve and somatic nerve; **9:** recurrent laryngeal nerve under the right subclavian artery)*

Cardiac Plexus (CP)

The CP (Figure 1) is formed by a wide net that inosculates the sympathetic and parasympathetic boughs, which we have studied before. The CP is situated at the base of the heart and is divided in a superficial portion and a deep portion. Although the reality of dissection shows that the mentioned anatomic division does not exist, even when there is an existent equivalent functional division and the existent structures are coronary, pulmonary, auricular and aortic, the superficial and deep diagram has survived through time, and that is why it will be described that way.

Superficial CP

It is situated under the aortic arch and in front of the right pulmonary artery. It is formed by the left sympathetic trunk's cardiac bough and the two cardiac branches of the cardiac vagus. In this plexus we can find a ganglion of major size, called *cardiac ganglion*. It sends branches to:

- the deep portion of the plexus
- the right cardiac plexus
- the anterior left pulmonary plexus.

Deep CP

It is located in front of the tracheal bifurcation, just over the pulmonary division; behind the aortic arch it is formed by sympathetic branches of the cervical ganglions and branches of the vagus and the recurrent. Arbitrarily, we can consider two parts:

- A half right: it sends boughs to the pulmonary right branch and to the right auricle (remember the region of the sinu-atrial node).
- A half left: it sends branches to the left pulmonary and the left atrium (LA), and it continues ahead to constitute the left cardiac plexus (see onwards).

At the same time, these two portions join again to originate a new order of fibers, which are distributed diagrammatically as following:

- A plexus which follows the territory of the right coronary artery,
- A plexus which follows the territory of the left coronary artery,
- A plexus that continues in the posterior face between the cava's venous pedicles and the pulmonary [2,3].

These fillets, which contain sympathetic and parasympathetic fibers, penetrate in the muscular walls by branches that remain in the epicardium, branches that go to the myocardium and branches that go to the endocardium [5].

Although the nervous distribution in the heart is complex, we can find nervous territories, mainly through the pneumogastric boughs and those that belong to the shattered ganglions. The right side fibers innervate the sinu-atrial node, whereas the left side fibers innervate the atrioventricular (AV) node.

Regarding the systems predominance on the nervous distribution, the auricles and the AV union possess a major number of parasympathetic fibers, whereas in the ventricles there is a prevalence of sympathetic fibers [6].

Cardiac efferent fibers

The double sense of innervation is one of the main characteristics of this system. The nerves that arrive to the heart do not only exert their function on it, but also they carry to the brainstem precise data about the muscle stretching's state (proprioceptive information). This information goes out the heart through fibers known as C fibers, which are amyelinic and arrive to the shattered ganglion without making any synapses on it; by the white communicant bough they go to the medulla and straight to the bulbar center. These references are connected with the perception of the cardiogenic pain. Although the cardiac muscle does not possess sensitive innervation as the pericardium does, some circumstances such as pain produced by a heart attack can be transmitted by these fibers and become conscious. Beside this, they play an important role in the tension of the arteries [5].

Shunt with the somatic plexus

All the fibers forming the different cardiac plexus present shunts with the cervical plexus, the brachial plexus and the intercostals nerves through communicating branches. These shunts have a great importance in the presence of pain in certain cardiac pathologies [2].

Functional anatomy of cardiac innervation in the perception of cardiac pain

The heart does not ache. However, the precordial pain is one of the most frequent reasons of admission to an emergency room [5].

The myocardial ischemia is a condition which is produced by a diminution in the blood contribution or an increase in the unsatisfied demand [6].

It is not exactly known how ischemia causes pain. A probable explanation could be that metabolic changes suffered by the myocardial cells would produce some "irritation" on the nervous fibers.

What is known for sure is the way of conduction of the cardiac pain (Figure 2). The painful stimulation traveling on the cardiac plexus (C fiber), without stopping on the shattered ganglion, goes through the communicating boughs to the cervical, brachial (internal cutaneous brachial) and the intercostal nerves. From now on, the sensitive route of these somatic nerves is used to conduct and make the pain conscious [3].

Therefore, the pain here is in the "referred" type and is known as angina pectoris. It is not located on a punctual sector but in a region that includes the mandible, the neck, the anterior surface of the thorax (sometimes also the posterior), both upper limbs and the epigastrium.

In past ages, the treatment of the ischemic pain was consisted in blocking (with local anesthesia and/or alcohol) and extirpating surgically the shattered ganglions. This leaded to feeling of recuperation because the pain disappeared and it produced some coronary vasodilatation, caused by the interruption of the sympathetic way. Nevertheless, the ischemia was not solved. Together with the best knowledge of coronary disease pathophysiology and the development of new medicines, this practice has been completely abandoned. The only thing left is the anecdotal part of the anatomic aspect.

Baroreceptor (BR) and Chemoreceptor's (QR) System

The BR and QR form a dependent system of the cardiac innervation that we've studied so far. This system has its own identity, and its physiology interacting narrowly with the cardiovascular system. Its function consists in informing the central nervous system (CNS) in real time (instantaneously) about the blood pressure state and the concentration of O_2 in blood. The CNS, thus, influences the heart rate and the arterial blood pressure.

Both BR and QR are cellular groups from ectodermic origin, also known as juxtagangliar. They are formed by the argentaffin type cells from the APUD system. They contain two cellular groups:

Glomic cells Type 1. They are cells containing granulations. They have a large nucleus and well developed organelles. It is possible to observe granules in their cytoplasm that contain catecholamines. Those cells are the ones directly interacting with the vessel.

Glomic cells Type 2. These cells do not possess inclusion granulations and they emit cytoplasmatic proyections that wrap the type 1 cells (for more information, please consult histology or neuroanatomy treatises cited) [7].

These cells, in which the one with major identity is the carotid body (see forwards), are distributed strategically in the aortic arch (actually, they are located in the entire aorta) and in the neck's vascular pedicle. They have mixed innervation, both sympathetic and parasympathetic. The latter is specially distributed by the vagus nerve (pair X).

The carotid body is a QR with elliptic form, and its size is approximately 7 x 4 mm. It is very frequent in the bifurcation of the primitive carotid. It is innervated by a branch of the glossopharyngeal nerve (pair IX) and by a thin plexus containing both sympathetic and parasympathetic fibers.

The efferents of these receptors reach the brainstem (solitary tract nucleus, nucleus ambiguus, dorsal nucleus of vagus nerve and the region known as vasomotor center of the bulbus, which belongs to the bulbar reticular formation). The afferent fibers reach these nuclei by the plexus we mentioned earlier [8].

Functional anatomy of cardiac innervation

The mechanical function of the heart is automatically generated by the cardionector system. However, the central nervous system modulates this activity in the form of a circuit, adapting its responses to the somatic or psychic instantaneous general conditions of an individual (dreaming/vigil; rest/effort; anger/

joy). The CNS is informed from the functional state of the heart (according to the blood pressure and the O_2 concentration in blood), and elaborates the responses to adapt those checked parameters with the reality, real or supposed, of the general soma. Moreover, it is in charge of taking certain painful information coming from the cardiac muscle (or the pericardium). All these actions are produced with hardly any conscious perception.

Nervous control of the blood pressure (BP), the heart rate (HR) and the concentration of O_2 in blood [9]

The BP depends on other variables such as the constriction state of the vascular arbor (vascular tone), the quantity of blood that the ventricle ejects by unit of time (volume minute) and the frequency of contraction in a minute (HR) (Figure 3). All that sensorial information enters the brainstem by the vagus, glossopharyngeus or by the ascendant fascicles of the spinal cord.

The autonomous centers of the CNS are:

- the bulbar reticular substance,
- the periventricular grey substance,
- the lateroventricular bulbar nuclei parvocelullaris and giantocelullar (these are activator nuclei),
- the paramedian nucleus, the ventral media complex and the raphe, these last two are inhibitors.

All these are grouped under the name of vasomotor centre of the bulb.

We have to add to this list the parasympathetic traditional nucleus, this is to say:

- the dorsal nucleus of vagus nerve,
- the nucleus of solitary tract, and
- the nucleus ambiguus.

It also exists a hypothalamic control of the BP and the HR performed by the anterior and posterior nuclei. The first are responsible of increasing the BP and the lasts of reducing it.

The QR and the BR constantly send inhibitor impulses to the vasomotor center. The only difference is the number of discharges per minute according the BP and the O_2 concentration. The lower are the triggers, the less inhibition of the vasomotor centre and vice versa (Figure 4).

A practical example of the physiology of this system: when an individual is staring on his feet, the venous return to the right heart decreases. Therefore the volume that will reach the left ventricle (LV) to expulse is lower and the BP falls slightly. This fall of the BP is noticed by the nerve fibers in the right atrium (RA) and the C fibers of the ventricle, apart from the arterial baroreceptors. The sympathetic influx to the heart increases, which produces an increase in the HR and a discrete vasoconstriction, whereas the parasympathetic discharge is reduced [10].

The opposite situation is observed when an individual takes a deep breath. The deep inspiration increases the venous return to the RA. Therefore that extra volume that reaches the LV is also noticed. As a response, the vasomotor center inhibits itself and the parasympathetic discharge is stimulated. Consequently, the BP and the HR decrease (Bezold-Jarisch reflex).

Another example with therapeutic application is the massage to the carotid sinus, located in the carotid bifurcation, which is projected a little lower the lower side of the mandible. When there is pressure on that area, an increase in the AT is simulated. As a response, using the same nervous route, there is an increase in the vagal note leading to decrease in the BP and HR. An extra data consists in the laterality that shows the conduction system's innervation. The right side stimulation has a stronger vagal influence on the sinu-atrial node and the left side's vagal stimulation has it on the AV node.

Special situations of the cardiac innervation [11]

The patients who have had a heart transplant are the ideal subjects for getting the functions (because of the lack) of the cardiac innervation. In this technique are only shunted the auricles (leaving the arrival of the cavas, the coronary sinus and the receptor's pulmonary veins) and the aorta and pulmonary extrapericardial arteries. Consequently, it is almost impossible to suture the ventricular nervous fillets or re-establish the intrinsic linking of the cardionector system. However, the rhythm is spontaneously re-established, even when it is eventually necessary to put a cardiac pacemaker (in 10 to 20 % of the cases). This way, the HR maintains itself almost invariable, independent of the somatic activity, and patients do not perceive the ischemic pain. There are some evidences of a transplanted heart's neo-innervation. Nevertheless, its consequences are still not understood, and they transcend the object of this review

Conclusion

The heart is an organ that functions independently from the nervous control. However, the central and peripheral nervous systems influence the stroke volume. The exquisite balance between the systems guarantees the amazing and complex cardiac performance.

On the one hand, the heart is in charge of the cardiac output and, on the other hand, the nervous system monitors the quality of the cardiac work by means of immediate measurement of CO_2 and blood pH.

Even though the cardiac nerve plexus branches do not conduct thermo-algesic sensitivity, they are capable of capturing changes in tissue irrigation (ischemia) and of turning them into referred pain sensations, thanks to their anastomoses with branches of somatic nerves.

When studying cardiac innervation, one studies a finished example of system cooperation.

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