

In Search of the Causal Mechanisms of Chest Pain

JUAN CARLOS KASKI,¹ DSC, MD, DM (HONS), FRCP, FESC, FACC, FAHA

Typical chest pain is often associated with myocardial ischemia, caused by atheromatous plaques that reduce coronary flow in certain myocardial regions. However, there are subgroups of patients who consult for typical pain on exertion, or are admitted to emergency care or chest pain units, in whom the angina pain is not associated with obstructive coronary artery disease. A proportion of these patients has “microvascular angina” (angina caused by coronary microcirculation dysfunction) (1) and in these cases—as in patients with obstructive coronary artery disease—, myocardial ischemia is responsible for angina pain. There is also a group of patients with typical chest pain that cannot be attributed to a specific cause or mechanism. These subjects are a complex issue, because therapies that are effective in patients with myocardial ischemia do not solve the problem in these cases. (2)

At present, pain management in general—and not only that associated with ischemia—is usually problematic, possibly due to the lack of knowledge on the pathophysiology of pain. Pain is a conscious experience that implies an “interpretation” of the effect a nociceptive stimulus has on the body. This interpretation is influenced by memories, emotional responses, impulse transmitters, ethnic and genetic factors, and cognitive status of the individual. There is not always a direct association between pain and the nociceptive impulse, nor does pain have a protective function in all cases. (3)

Since pain is a subjective experience involving many components, there is a huge and complex network in the nervous system to “process” pain. This brain network is often known as the “pain matrix” and includes—in simple words— sensory-discriminative and cognitive-affective areas (4), which have been thoroughly investigated in the last two decades due to the availability of improved imaging techniques and other major technological developments.

In this issue of the Journal, Ochoa et al (5) present

the results of a small prospective, comparative study on women with cardiac syndrome X (typical chest pain in the absence of obstructive coronary artery disease), women with documented coronary artery disease, and a control group including women without any known cardiac disease. The main purpose of this work was to investigate the anatomic characteristics of afferent pathways that convey nociceptive impulses, producing a sensation of chest pain in patients with syndrome X and in those with coronary artery disease. To this end, the authors used a diffusion MRI tractography technique, which allows studying the two primary somatosensory pathways in vivo: the medial lemniscus and the lateral spinothalamic (LST) tract. Ochoa et al (5) have compared the characteristics and integrity of the LST tract and its thalamocortical fibers in patients with syndrome X and in those with coronary artery disease.

Tractography—used in neuroscience—is a three-dimensional modeling technique used to visualize neural tracts using data collected by diffusion tensor imaging. Its use has been briefly commented in Ochoa’s article (5). It combines special techniques of magnetic resonance imaging and computer-based image analysis. (6) In addition to the long tracts that connect the brain with the rest of the body, there are complex neural networks, made up of shorter connections, among different cortical and subcortical regions. These special fiber tracts cannot be identified with current imaging techniques but are detected with tractography. With this technique, the resonance sequences are used to set the “symmetry” of water diffusion in the regions of interest. Water diffuses evenly in all directions in so far no barriers prevent such diffusion (isotropic diffusion). However, if water spreads in regions with “barriers”, diffusion will be asymmetric; this asymmetry is called “anisotropy”. The special fibers in conducting tracts direct water diffusion asymmetrically, with predominance of the major axis, parallel

Rev Argent Cardiol 2013;81:96-97. <http://dx.doi.org/10.7775/rac.v81.i2.2320>
SEE RELATED ARTICLE: <http://dx.doi.org/10.7775/rac.v81.i2.596>. Rev Argent Cardiol 2013;81:119-124.

Address of reprints: Professor J. C. Kaski - Cardiovascular Sciences Research Centre SGUL - Cranmer Terrace, London SW17 0RE UK
Email: jkaski@sgul.ac.uk

¹ Director, Cardiovascular Sciences Research Centre, St. George’s, University of London, London, UK

DSc Doctor of Science

MD Medical Doctor

FRCP Fellow of the Royal College of Physicians

FESC Fellow of the European Society of Cardiology

FACC Fellow of the American College of Cardiology

FAHA Fellow of the American Heart Association

Cardiovascular Sciences Research Centre SGUL - Cranmer Terrace, London SW17 0RE UK - e-mail: jkaski@sgul.ac.uk

to the fiber pathway (“tensor”). In the white matter, the main barrier to water diffusion is the axon myelin. The axonal tracts show resistance to perpendicular water diffusion, and present a channel for diffusion parallel to the direction of the fiber pathway. The use of this technique has offered many possibilities to investigate neurophysiological processes, including research on pain transmission. (7)

Ochoa et al (5) found no differences in the physical characteristics of the tracts, but they did find a significant difference in the number of voxels in the three groups of patients analyzed. This study (5), in a reduced group of patients and healthy controls, is not strong enough to draw specific conclusions regarding the nature or mechanisms of chest pain in patients like the ones included in the study. However, its greatest worth is to have demonstrated that it is possible to assess neurological tracts involved in pain transmission in this group of patients, and to have opened up an interesting line of research in this field. Pain is very difficult to investigate and manage due to its complexity. To understand the nature and mechanisms of chest pain in patients with angina –with or without coronary artery disease– is one of the most important challenges that clinical cardiologists have to face today. Knowing these mechanisms would probably lead to the development of more effective strategies than those currently implemented for patient

management, many of whom have a very poor quality of life due to the presence of angina pain, often unrelated to myocardial ischemia.

Conflicts of interest:

None declared.

REFERENCES

1. Herrmann J, Kaski JC, Lerman A. Coronary microvascular dysfunction in the clinical setting: from mystery to reality. *Eur Heart J* 2012;33:2771-81
2. Kaski, JC. Pathophysiology and management of patients with chest pain and normal coronary arteriograms (cardiac syndrome X). *Circulation* 2004;109:568.
3. Apkarian AV, Bushnell MC, Treede RD, Zubieta JK. Human brain mechanisms of pain perception and regulation in health and disease. *Eur J Pain* 2005; 9: 463–84
4. Albe-Fessard D, Berkley KJ, Kruger L, Ralston HJ, III, Willis WD, Jr. Diencephalic mechanisms of pain sensation. *Brain Res* 1985;356:217-96
5. Ochoa JP, Resnik LM, Siarresi EA, Garate ML, Princich JP, Binahi D et al. Spinothalamic Assessment by Magnetic Resonance Tractography. *New Contributions in the Pathophysiology of Pain in Patients with Syndrome X. Rev Argent Cardiol.* 2013;81:119-124. <http://dx.doi.org/10.7775/rac.81.i2.596>
6. Le Bihan D, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. *Radiology* 1986;161:401-407.
7. Kamada K, Sawamura Y, Takeuchi F, et al. Functional identification of the primary motor area by corticospinal tractography. *Neurosurgery* 2005;56:98-109