ESC European Society of Cardiology

European Heart Journal Open (2023) **3**, 1
https://doi.org/10.1093/ehjopen/oead063

CORRESPONDENCE
Coronary artery disease

Is electrical neuromodulation able to affect the extent and stability of coronary atheromatous plaques?

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Received 17 April 2023; revised 9 May 2023; accepted 8 June 2023; online publish-ahead-of-print 16 June 2023

Handling Editor: Magnus Bäck

To the Editor

We read with interest the thorough review article on neuromodulation in patients with refractory angina pectoris, by Fabienne Vervaat and colleagues published in the January 2023 issue of European Heart Journal Open.[1] In addition to the mechanisms presented, it may be relevant to pay attention to recent very intriguing developments in the role of the nervous system in the vascular and the immune systems that may impact on the perception of neuromodulation as a therapy and its possible effect on atheroma plaques. Mahanta and colleagues found in apolipoprotein E–deficient ($Apoe^{-/-}$) mice that the density of both sensory and sympathetic nerve fibres was abundant in the aortic adventitia and these were greatly increased in areas of atherosclerotic plaques.[2] Using virus tracing techniques, they showed that these fibres establish a structural artery–brain circuit (ABC) with the sensory arm entering the CNS via dorsal root ganglia in the spinal cord and which connect to higher brain regions. The efferent arm of the ABC projects from hypothalamic neurons back to the adventitia via bifurcated projections involving the parasympathetic and the sympathetic nervous system. In addition, running in parallel, there has been an explosion in knowledge about the effect of the nervous system on immunology. Mahanta *et al*. coined the term 'neuroimmune cardiovascular interfaces' (NICIs) in atherosclerosis-diseased adventitia segments. Inflammatory products can stimulate axons, and efferent neuronal activity can stimulate or suppress various immune mediators. Thus, the nervous system may contribute to cardiovascular atherosclerotic disease progression, either directly through innervation of specific layers of the endothelium of the cardiovascular system or indirectly by influencing the immune responses involved in the development of cardiovascular pathology, especially atheroma. Finally, an important observation was that coeliac ganglionectomy reduced disease progression in the aorta, norepinephrine levels, and plaque size and stabilized plaque vulnerability.[2]

As Vervaat and colleagues confirm in their paper, spinal cord electrical stimulation (SCS) or neuromodulation can reduce the complaints of intractable angina and reduce myocardial ischaemia.[1] In part, this is explained by the 'gate theory of pain', but other factors on the efferent side are also operating. There is a decrease in sympathetic activity independent of the reduction of pain, a redistribution of myocardial blood flow through opening collaterals, and release of myocardial endorphins. In the early days in the use of this technique, there was concern that the inhibition of pain might allow ischaemia to continue potentially leading to lethal arrhythmias. However, several studies showed that there did not appear to be any rise in mortality and even a suggestion of a reduction.[3] A remarkable study done by Mannheimer *et al*. in 1998[4] compared epidural spinal cord stimulation to coronary artery bypass grafting in high-risk patients and showed that CABG and SCS appear to be equivalent in terms of symptom relief after 6 months and on an intention to treat basis the mortality was lower in the SCS group. Cerebrovascular morbidity was also lower in the SCS group.

The question is, therefore, could SCS affect coronary artery plaques, leading to plaque stability and perhaps reduced plaque size similar to the effect of coeliac ganglionectomy as reported in the experimental model above?[2] Mahanta *et al*. suggest, when discussing potential therapies, that the use of bioelectronics neuromodulation should be explored. The technique, i.e. SCS, is already available, and it may help reduce mortality of patients with severe coronary artery disease, in addition to relieving their symptoms. Further studies of SCS impact on plaque morphology and stability are warranted.

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Funding

None declared.

Conflict of interest: None declared.

Data availability

No new data were generated in support of the article.

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