

Review of: "From Psychostasis to the Discovery of Cardiac Nerves: The Origins of the Modern Cardiac Neuromodulation Concept"

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Potential competing interests: No potential competing interests to declare.

Comments to the manuscript

„From Psychostasis to the Discovery of Cardiac Nerves: The Origins of the Modern Cardiac Neuromodulation Concept“ by Beatrice Paradiso et al.

This manuscript is a thoughtful and philosophically inspired comprehensive account of mystical, religious, and scientific ideas on the heart. It covers about 5000 years, from ancient Egypt to the present, quoting some references that are usually not found in the neurocardiological literature. It is well suited to enrich the scope of contemporary (neuro-)cardiologists' ideas. I have but one major and a few minor points to comment on.

Major:

The main text is partly redundant and thus cumbersome to read. For example, the last paragraph on p31 is largely redundant to p19. I suggest cross-checking the manuscript for similar redundancies in order to make it more concise.

Minor:

1. Galenus of Pergamon spent most of his life in the 2nd century CA (129-209) and not in the 3rd century CA.
2. P20, 2nd para: GABAergic neurons in the caudal VLM receive excitatory input from the NTS and in turn inhibit glutamatergic pre-sympathetic neurons in the rostral VLM. Please use caudal and rostral VLM, respectively, throughout instead of „distal“ or „upper“ VLM.
3. P24, 3rd para: How good is the evidence for preganglionic sympathetic neurons projecting directly to intrinsic cardiac ganglia (cf. also Fig. 11)? Only in this case was it meaningful to speak of „postganglionic sympathetic neurons“ in cardiac ganglia. On p29, para 4, such intramural sympathetic neurons were not mentioned.
4. Figs 12 and 14: Why are contacts of nodose afferent neurons to SIF cells in cardiac ganglia omitted? Such highly interesting connections were described by Cheng et al. (JCN 1997, 381:1-17).
5. Legend to Fig. 12: Nitroergic interneurons in the DNV presumably act within and not „surrounding“ the nucleus. By the way, please use nNOS (neuronal nitric oxide synthase) throughout instead of „nNO“ for designating nitroergic neurons.
6. On p29, please specify that most **cardiac** ganglion cells use acetylcholine.
7. P34, top: How is the synergistic interplay of the sympathetic and parasympathetic systems in „urine production“

meant? Possibly better „urine storage and release“ or similar.

8. Legend to Fig. 14: Do nitregeric neurons of cardiac ganglia really project to the brainstem? This sentence is probably misleading. Or were nitregeric neurons in the NTS or trigeminal nucleus meant? Why do AMB axons end at the heart hilum with a question mark and do not continue to cholinergic cardiac ganglion neurons?

Typos:

P19, 2nd para: acquires

P20, 2nd para: viscerotopically

P20, 3rd para: rhythmic

P24, 2nd para: connexon channels