Author/s:
Furness, JB

Title:
The physiological relevance of constriction of mesenteric arteries by topically applied noradrenaline

Date:
2017-11-01

Citation:
Furness, J. B. (2017). The physiological relevance of constriction of mesenteric arteries by topically applied noradrenaline. Journal of Physiology, 595 (21), pp.6783-6784. https://doi.org/10.1113/JP275097.

Persistent Link:
https://hdl.handle.net/11343/293808

Letter to the editor, Journal of Physiology

From:

John B Furness[1,2]

[1]*Florey Institute of Neuroscience and Mental Health, Parkville, Victoria 3052, Australia*

[2]*Department of Anatomy & Neuroscience, University of Melbourne, Parkville, Victoria 3010, Australia*



**The physiological relevance of constriction of mesenteric arteries by topically applied noradrenaline**

The mesentery is an attractive substrate for direct observation of small blood vessels in living animals and many investigations of blood vessel physiology and responsiveness to drugs in the exposed mesentery have been published, including in this journal (Landis 1930; Zintel, 1936; Zweifach, 1954; Furness & Marshall, 1974; Hébert and Marshall 1985). The methods have in common exteriorising a loop of intestine with its associated mesentery and blood vessels, and visualising regions of interest under a microscope. Moreover, because the mesentery can be easily prepared histologically as a wholemount, different cellular components can be mapped, including the distribution of vascular innervation, which has been related to vascular responses to nerve activity and neurotransmitter, including noradrenaline, actions (Furness, 1973, Furness & Marshall, 1974). In a recent issue of this journal, Nyvad et al. (2017) describe direct observations of changes in diameter and flow in small arteries of the rat mesentery, in response to agonists, using the methods previously described. To restrict drug exposure to vascular segments, mesenteric vessels were passed through a small chamber that was sealed with vacuum grease where the vessels entered and left.

Nyvad et al. (2017) investigated mesenteric arteries with internal diameters of approximately 150-300 µm and found that these vessels were constricted by local application of noradrenaline, with a threshold of around 100 nM and a half maximal effect at about 1 µM. In an earlier publication in this journal, the effects of local application of noradrenaline (as the bitartrate) were

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1113/JP275097.

compared between arteries of different diameters, from 12 to 350 µm in diameter (Furness & Marshall, 1974). The larger vessels (80-350 µm in diameter, referred to as principal arteries) had thresholds of about 100 nM and a half maximal effect at about 1µM, in agreement with the recent paper. However, smaller arteries were more sensitive, and the smallest muscular arteries (12-22 µm in diameter) were about 10 fold more sensitive than the principal arteries. The earlier paper also reported that the larger arteries were slightly dilated by 3 nM noradrenaline. Veins constricted, but were much less sensitive than the arteries, and capillary vessels did not change diameter.

In a further study of the directly observed responses of rat mesenteric arteries to noradrenaline that was published in this journal, Hébert and Marshall (1985) investigated effects of circulating noradrenaline, sufficient to raise blood pressure by 25-75 mmHg. They found that terminal arteries and precapillary arterioles (< 30 µm in diameter) were constricted but the larger arteries dilated slightly at the peak of the blood pressure increase. The observations of Hébert and Marshall (1985) are consistent with the view that it is constriction of the smaller arteries that contributes most to increased vascular resistance and blood flow regulation (Folkow & Neil, 1971). Direct measurement of pressures in arterioles of the mesentery *in vivo* support this view, the greatest pressure drop being between terminal arteries of 30-40 µm diameter and the capillaries (Richardson & Zweifach, 1970). Thus although principal arteries are constricted by local, topical, application of noradrenaline (Furness & Marshall, 1974; Nyvad et al 2017), this is not their reaction when blood-borne noradrenaline reaches the mesenteric arterial tree (Hébert & Marshall, 1985).

Thus the physiological relevance of reactions of principal arteries in the rat mesentery, generally in the diameter range 80-350 µm (Furness & Marshall, 1974; Hébert & Marshall 1985), that were reported in the recent paper, needs to be considered in relation to the responses of vessels at other levels in the vascular tree, especially when vessels at other levels have been studied using similar methods in the same vascular bed in the same species. In particular, reactions to locally applied noradrenaline may not match the physiological effects of circulating noradrenaline. On the other hand, the vessels that are most responsive to applied noradrenaline, the mesenteric precapillary arterioles, are not innervated (Furness, 1973) and do not respond to nerve stimulation (Furness & Marshall, 1974) and, likewise, the arterial innervation in the wall of the intestine becomes sparse or absent as the smallest vessels, generally less than 30 µm in diameter, are reached (Furness, 1971). In contrast, nerve stimulation at 0.5 to 6 Hz constricted principal arteries, reducing their diameter by up to 60% (Furness & Marshall, 1974). It is interesting.

In conclusion, physiologically relevant responses of mesenteric arteries to circulating noradrenaline differ from those observed in reaction to topical application of noradrenaline. Moreover, responses to circulating noradrenaline differ from those observed when vasomotor nerves are stimulated.

Conflicts: The author declares no conflict of interest

**References**


Folkow B & Neil E. (1971). *Circulation*. Oxford University Press, London.

Furness JB. (1971). The adrenergic innervation of the vessels supplying and draining the gastrointestinal tract. *Z. Zellforsch.* **113,** 67-82.

Furness JB. (1973). Arrangement of blood vessels and their relation with adrenergic nerves in the rat mesentery. *J. Anat.* **115,** 347-364.

Furness JB & Marshall JM. (1974). Correlation of the directly observed responses of mesenteric vessels of the rat to nerve stimulation and noradrenaline with the distribution of adrenergic fibres. *J. Physiol. (Lond)* **239,** 75-88.

Hébert MT & Marshall JM. (1985). Direct observations of responses of mesenteric microcirculation of the rat to circulating noradrenaline. *J. Physiol. (Lond)* **368,** 393-407.

Nyvad, J, Mazur A, Postnov DD, Straarup MS, Soendergaard AM, Staehr C, Brøndum E, Aalkjaer C & Matchkov VV. (2017). Intravital investigation of rat mesenteric small artery tone and blood flow. *J. Physiol. (Lond)*. **595,** 5037–5053.

Richardson DR & Zweifach BW. (1970). Pressure relationships in the macro and microcirculation of the mesentery. *Microvasc. Res.* **2,** 474-488.

Zintel HA (1936). A new transparent chamber for exteriorizing a loop of intestine and its mesentery. *Anat. Rec.* **66,** 437-447.

Landis EM. (1930). The capillary blood pressure in mammalian mesentery as determined by the micro-injection method. *Am. J. Physiol.* **93,** 353-362.

Zweifach, BW (1954). Direct observation of the mesenteric circulation in experimental animals. *Anat. Rec.* **120,** 277-291.