Evolutionary aspects of neural control of coronary blood flow

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An evolutionary perspective of the autonomic nerves and their many transmitters innervating the coronary circulation is reasonably well described, but the functional significance of this anatomy is poorly understood. This is a fertile area for investigation, given the poor oxygen reserve for defence normally in the myocardium, and the morbid impact of obstructive coronary disease. However, among mammalian species including man, Gregg & Fisher (1963) point out that the course and distribution of the major coronary arteries is remarkably similar. Intergroup differences are less pronounced than intragroup variations. Nevertheless, despite this anatomical knowledge, there is little systematic comparative data concerning functional neural control of coronary blood flow among mammalian species, and what exists implies that neural control of the coronary circulation differs between species. The enigma is manifest by the variable findings with acetylcholine *e.g.*, Kalsner (1985) in his review, concluded that coronary resistance vessels from most species constrict in response to acetylcholine, and that the dog was the only species where coronary vessels dilate. Also, the diving seal constricts the circumflex bed possibly by atropine sensitive pathways (Elsner *et al.*, 1985). In the midst of this uncertainty, one would think a successful design in evolutionary terms for neural coronary blood flow control in one mammalian species would be present in others. Finally, there is still a general assumption, probably erroneous (see below, Quail *et al.*, 1996; White, 1998), that autonomic control of the different myocardial regions supplied by the right, circumflex and anterior descending coronary arteries, is uniform in effect.

Recently, we noted in the awake dog that baroreflex regulation of coronary blood flow and conductance varies between the left coronary beds when aortic pressure rises (Quail *et al.*, 1996; White, 1998). Moreover, we were surprised to find that while baroreflex augmentation of coronary conductance appeared small in the face of loading the left ventricle, the quantitative neural effects were quite large when unmasked by the appearance of a strong constrictor response to the same stimulus following pharmacological autonomic blockade of cholinoceptors, α_1-, α_2-adrenoceptors, and β_1-, β_2-adrenoceptors ("total autonomic block", TAB). In other words, the underlying myogenic constrictor response of the coronary vessels to an aortic pressure rise appears to dominate dilator metabolic effects, and in the absence of baroreflex-induced flow augmentation, the rise in blood flow is less than when the autonomic receptor mechanisms are intact. This may be important given the poor oxygen reserve in the coronary beds. Therefore, in the process of defence against multiple environmental stimuli normally confronting mammals, important reflex dilator neural factors prevail over constrictor factors. This is an interaction effect, largely hidden from experimental gaze in bench studies, and in less sensitive physiological models where anaesthetic agents themselves variably block pathways actually being sought.

In order to investigate baroreflex regulation among mammalian species, we recently compared the responses of awake dogs, with those in awake sheep (see Hamut *et al.*, this issue). Interestingly, the results show that in the regions supplied by the circumflex and anterior descending coronary arteries, the baroreflex pattern of effect across the beds in sheep is qualitatively similar to that of the dog. However, the quantitative effects in sheep are less than in the dog. The main similarity between species is the neural augmentation flow effect in the circumflex bed when aortic pressure rises. In the sheep this amounts to 136% of control at 8s in the intact animal, but is significantly less at 124% following TAB. These effects are relatively less in the anterior descending bed, and not apparent in the right coronary bed. The quantitative role of the different receptor classifications and their interactions within the neural control 'TAB' examined in these studies, and the role of other (residual) neural mechanisms, remains to be elucidated. It is concluded that the baroreflex patterns of neural control in different left coronary beds are qualitatively similar in dogs and sheep. This suggests that a common evolutionary pattern of neural control has emerged, within mammalian species.

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