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Autonomic control of circulation in fish: A comparative view

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ABSTRACT

The autonomic nervous system has a central role in the control and co-ordination of the cardiovascular system in all vertebrates. In fish, which represent the largest and most diverse vertebrate group, the autonomic control of the circulation displays a vast variation with a number of interesting deviations from the typical vertebrate pattern. This diversity ranges from virtually no known nervous control of the circulation in hagfish, to a fully developed dual control from both cholinergic and adrenergic nerves in teleost, much resembling the situation found in other vertebrate groups. This review summarizes current knowledge on the role of the autonomic nervous system in the control of the cardiovascular system in fish. We set out by providing an overview of the general trends and patterns in the major fish groups, and then a summary of how the autonomic nervous control is involved in normal daily activities such as barostatic control of blood pressure, as well as adjustments of the cardiovascular system during feeding and environmental hypoxia.

1. Introduction

The cardiovascular system is a central component in the physiological machinery that maintains homeostasis of the animal body. Its most fundamental function is to supply oxygen and nutrients to the tissues, and to remove metabolic wastes produced in cellular metabolic processes. The main driving force to circulate the blood is provided by the arterial blood pressure generated by the beating heart, while local control of blood flow largely relies on changes in arteriolar resistance. In the vast majority of vertebrates, the rate and force of cardiac contraction, and the control of vascular resistance, are directly determined by input from the autonomic nervous system (Nilsson, 1983, 1997; Morris and Nilsson, 1994). In fish, the general function of the cardiovascular system does not represent any major deviations from this general picture, but the autonomic nervous control of the cardiovascular system displays a number of interesting and important differences from the general vertebrate scheme.

The typical piscine circulatory system is composed of a single heart connected in series with the gills where respiratory gas exchange occurs. The heart is a four-chambered structure with the single *sinus venosus*, atrium, ventricle and *bulbus arteriosus* connected in series and enclosed in a pericardial cavity (Farrell and Jones, 1992). However, as will be evident below, several more or less dramatic variations from this pattern exist among fishes, with the multiple hearts in hagfishes and the profound circulatory adaptations for aerial respiration in lungfishes as notable exceptions. Most fish are strictly ectothermic with a comparatively low metabolic rate. Yet, their oxygen uptake is a relatively costly process as most fish exclusively obtain oxygen from water, which compared with air, has a much higher density (approx. 1000 times) and viscosity (35–100 times depending on temperature). Furthermore, the oxygen content of water is low with a maximum of around 10 ml of oxygen per liter of water at 0 °C compared to around 210 ml per liter for air. Due to temperature factors, slow rates for oxygen diffusion in water and oxygen depletion caused by oxidative processes, oxygen poor conditions (hypoxia) frequently occur in aquatic environments further complicating oxygen uptake. Additionally, since water has a density similar to blood, the gravitational impact on the cardiovascular system is minimal in water compared with terrestrial habitats. Thus, before land was colonized by vertebrates, the selection

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pressures shaping the evolution of the vertebrate cardiovascular system were those of an aquatic environment where cardiovascular challenges differed considerably from those experienced by terrestrial animals (Dejours, 1975).

The aim of the following review is to summarize current knowledge on autonomic nervous control of the cardiovascular system in fish. The denomination "fish" is typically used to describe a loosely related group of mostly ectothermic and aquatic craniates with fins that retain their gills throughout development. While fish do not form a monophyletic group in a strict taxonomic sense like e.g. birds and mammals, it is customary to categorize this diverse group into the four main sub-groups: cyclostomes (hagfish and lampreys), elasmobranchs (e.g. sharks and rays), dipnoans (lungfish), and teleosts (bony fishes). Although this classification may be questioned from a taxonomic point of view, it is practical from a comparative physiological standpoint as these groups possess a number of common unique features in terms of circulatory physiology and autonomic control. Thus, for convenience and ease of comparison with existing literature, the traditional classification has been retained in the following account. Consequently, the review starts by describing the general trends and patterns of autonomic cardiovascular control in the main groups of fishes, primarily focusing on classical adrenergic and cholinergic control systems. Recently, knowledge has expanded considerably regarding the role of gasotransmitters and neuropeptides in cardiovascular control in fish. While this subject is only briefly mentioned in the following account, several excellent reviews are available on this topic (see for example Morris and Nilsson, 1994; Olson, 2009; Olson and Donald, 2009; Tota and Cerra, 2009). Furthermore, recent years have seen a shift in the focus of research on autonomic control of the circulation in fish. By moving from largely descriptive pharmacological studies in the past, new contributions have focused more on the integrated role of the autonomic nervous system in reflex responses to changes in the internal or the external environment, such as during blood pressure changes (i.e. the baroreflex), chemoreceptor-reflexes resulting from environmental hypoxia, as well as, from mechanical and chemical stimuli on the gastrointestinal tract during feeding.

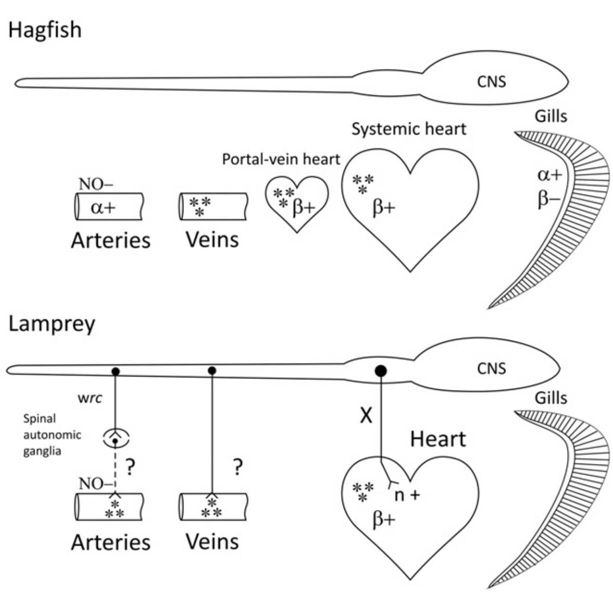

Fig. 1. Simplified diagram showing a general overview of the autonomic innervations and control of the heart (hearts), systemic and branchial vessels in cyclostomes. Preganglionic nerves are depicted as solid lines and post-ganglionic neurons are depicted as broken lines. Legend: CNS, central nervous system; w*rc*, white *rami communicates*; X, vagus nerve; ?, unidentified or suggested pathways; +, vasocontrictory or positive chronotropy; −, vasodilatory or negative chronotropy; NO, nitric oxide; α, alpha-adrenoceptor; β, beta-adrenoceptor; n, nicotine receptor; * indicates chromaffin cells.

2. Cyclostomes

The cyclostomes, comprising Petromyzontids (lampreys) and Myxinoids (hagfishes), are a loosely related group of primitive jawless fishes. There are striking differences in cardiovascular morphology and physiology between these two groups, as comprehensively summarized by Forster et al. (1991) and Farrell (2007a). For example, while the lampreys have a single heart like all other fish, the hagfish circulation includes a systemic (branchial) heart and three accessory hearts, of which the portal-vein heart is the only that is composed of myocardial tissue (Fänge et al., 1963). A brief overview of the nervous control of the cardiovascular system in cyclostomes is presented in Fig. 1.

2.1. Heart

The lamprey heart receives cholinergic vagal innervation (Augustinsson et al., 1956), while the hagfish heart(s) is functionally aneural (Greene, 1902; Carlsson, 1904; Augustinsson et al., 1956; Hirsch et al., 1964; Jensen, 1965). The systemic and the portal-vein heart, as well as the walls of the posterior cardinal veins in hagfish contain large quantities of catecholamine containing cells, but these cells do not appear to be controlled by extrinsic nerves (Augustinsson et al., 1956; Euler and Fänge, 1961). Nevertheless, carbachol and serotonin stimulated catecholamine release in a perfused posterior cardinal vein/systemic heart preparation in the Atlantic hagfish (*Myxine glutinosa*), but the authors concluded that a neural mechanism was unlikely (Bernier and Perry, 1996). A β-adrenergic tonus is clearly important for normal cardiac function in hagfishes, because a pronounced bradycardia is observed in isolated systemic and portal hearts following catecholamine depletion with reserpine (Bloom et al., 1961) and β-adrenergic blockade with sotalol (Johnsson et al., 1996; Johnsson and Axelsson, 1996). Adrenaline increases heart rate and stroke volume *in vivo* in hagfish, while sotalol has a negative chrono- and inotropic effect (Axelsson et al., 1990).

Vagal stimulation and administration of acetylcholine in lampreys lead to cardioacceleration through stimulation of cardiac nicotinic receptors (Carlsson, 1906; Augustinsson et al., 1956; Falck et al., 1966; Lukomskaya and Michelson, 1972). This is a peculiar response that contrasts with the typical cardioinhibitory response to vagal stimulation of all other vertebrates. There is no clear evidence for a functional adrenergic innervation of the heart in lampreys (Dahl et al., 1971), but similar to the situation in hagfish, cells with catecholamine-containing granules are present in the myocardium and vasculature (Augustinsson et al., 1956; Dahl et al., 1971; Shibata and Yamamoto, 1976; Epple et al., 1985). The function and control of catecholamine release from these cells are poorly understood. Isolated lamprey hearts respond to adrenaline, noradrenaline and tyramine with positive inotropism and chronotropism through a β-adrenoceptor mediated mechanism (Augustinsson et al., 1956; Falck et al., 1966; Lukomskaya and Michelson, 1972); and both adrenaline and noradrenaline induce tachycardia *in vivo* in the lamprey *Geotria australis* (Macey et al., 1984). In more recent studies it has been shown that adrenocorticotropic hormone (ACTH) released from the pituitary during stress may trigger the release of stored catecholamines (Bernier and Perry, 1996). Serotonin stored within the cardiac chromaffin cells may also elicit catecholamine secretion in an autocrine or paracrine fashion (Bernier and Perry, 1996).

2.2. Vasculature

The existence of vasomotor nerves in hagfish is uncertain (Forster et al., 1991). While adrenaline had no effect on branchial resistance in the hagfish *in vivo*, systemic resistance was slightly reduced but this was speculated to be a passive effect of increased cardiac output and arterial blood pressure (Axelsson et al., 1990). Adrenaline and noradrenaline increased systemic vascular resistance in perfused preparations of the Atlantic hagfish, a response that was inhibited following