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Review

Autonomic control of glands and secretion: A comparative view

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ABSTRACT

The autonomic nervous system together with circulating and local hormones control secretion from glands. This article summarizes histochemical and functional studies on the autonomic innervation and control of secretory glands in non-mammalian vertebrates, including secretion of saliva in the mouth and gastric acid in the stomach, secretion of enzymes and bicarbonate from the pancreas and gut wall, secretion of mucus in the gut epithelium and onto the skin, and salt secretion from salt glands and rectal glands. Cholinergic and adrenergic nerves, directly or indirectly, in combination with different types of peptidergic and other nerves appear to innervate gland tissues and affect secretion in all investigated species.

Contents

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1. Introduction

Most secretory events in a vertebrate are associated with the gastrointestinal canal and with the processing of food. This includes secretion from the salivary glands in the mouth, from mucous glands all along the gut, from oxyntic and peptic gastric glands, from the pancreas and from small glands in the intestinal wall. The glands are all controlled by multiple factors with the autonomic nervous system playing a prominent part. Secretion of mucus in the airways or onto the skin, tears, sweating and secretion of wax are other secretory mechanisms involving the autonomic nervous system.

The "thumb rule" for autonomic control of secretory mechanisms is that parasympathetic pathways, in particular cholinergic nerves, stimulate secretion. Sympathetic, adrenergic pathways mainly have their effect through regulation of the blood flow through the glandular tissue (see Sandblom and Axelsson, 2010—this volume, for control of circulation by the autonomic nervous system). Peptidergic transmitters and cotransmitters, as well as nitrergic and possibly purinergic nerves are involved in the control to different degrees, as are several circulating or locally released hormones. In the gut, activities in the enteric nervous system are tightly integrated in the control mechanisms.

Our knowledge of the control mechanisms is based on the mammalian systems, and with few exceptions, the information on non-mammalian vertebrates is scattered and patchy. Also, the distinction between the parasympathetic and sympathetic systems is not as clear in non-mammalian vertebrates as in mammals, with no distinct parasympathetic outflow from the sacral region of the spinal cord (see Nilsson, 2010—this volume). Different aspects on gut secretion and its control in non-mammalian vertebrates have been previously reviewed by Smit (1968), Jönsson (1994) and Holmgren and Holmberg (2005). The aim of this text is to update available information on the involvement of the autonomic nervous system in the control of non-mammalian secretory systems, stressing similarities and differences in the control systems. However, there are still too wide gaps in our knowledge to allow more than speculations on evolutionary trends.

2. Secretion of saliva

Saliva is a watery solution of electrolytes, enzymes and antibacterial substances, secreted into the mouth cavity from salivary glands. Secreted saliva also contains mucus (for secretion of mucus from salivary glands and other glands along the gut, see Section 6).

Salivary glands are found in all terrestrial vertebrate groups. In addition to important functions in lubricating the food, and initial enzymatic digestion, saliva plays a role in taste, vocalisation and buffering pH in the mouth cavity. In its extreme, saliva may be used for capturing food (the sticky tongue of a woodpecker), making nests (swifts and swallows) or killing—the poison glands of snakes are modified labial salivary glands (Tucker, 2007).

Anatomically, the salivary glands in the mouth region of non-mammalian tetrapods are innervated by cranial (parasympathetic) pathways running in branches of the facial nerve (VII) and to some extent the glossopharyngeal (IX) cranial nerve (see Nilsson, 1983; Gibbins, 1994). Spinal (sympathetic) fibres running in the sympathetic chains may join the cranial nerves and innervate the glands.

Very little is known of the regulatory mechanisms in the control of salivary secretion in non-mammals. The innervation is presumably cholinergic with an adrenergic component, similar to mammals. In a series of light and electron microscopy experiments on salivary glands from amphibian *Rana* species, Iwasaki and coworkers demonstrate that secretion from lingual glands (and lingual epithelium) can be elicited both with cholinergic and adrenergic agents (e.g. Iwasaki et al., 1997, using the Tokyo Daruma frog, *Rana porosa porosa*; Fig. 1). Similar to mammals, cholinergic stimulation causes a release of fluid

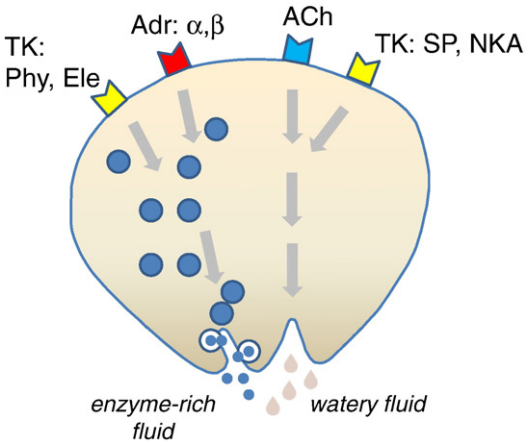

Fig. 1. Schematic picture of the control of secretion from salivary glands in an amphibian. Note the differential effect of cholinergic and adrenergic drugs on secretion of a watery fluid (right half of figure) and exocytosis of electron-dense vesicles (enzyme, protein-containing; left half of figure), respectively. The two secretion mechanisms also show different sensitivities to tachykinins. ACh, acetylcholine; Adr, adrenergic drugs; Ele, eledoisins; NKA, neurokinin A; Phy, physalaemin; SP, substance P; TK, tachykinin). Compiled from results of studies on the Tokyo Daruma frog, *Rana porosa porosa* by Iwasaki et al., 1997, 1998.

(demonstrated as a reduction in the volume of cytoplasm), while adrenergic stimulation with both an α-adrenergic (phenylephrine) and a β-adrenergic (isoprenaline) agent causes exocytosis of electron-dense granules (presumably proteins). All effects were blocked by an appropriate specific antagonist. In a further study, it was shown that tachykinins also may stimulate saliva secretion. Interestingly, the more generally occurring neuronal tachykinins substance P and neurokinin A (NKA) mainly evoke a secretion of salivary fluid, while the amphibian skin tachykinins physalaemin or the cephalopod peptide eledoisin both were more potent in causing exocytosis of electron-dense granules. Like in mammals, the effect of substance P and NKA mimicked that of cholinergic drugs (Iwasaki et al., 1998; Fig. 1).

3. Secretion of gastric acid and pepsinogen

Gastric acid and pepsinogen are, together with mucus, the dominating secretory products of the vertebrate stomach. Secretion of gastric acid is almost the only secretory mechanism in the gut where comparative studies of non-mammalian vertebrates have been performed to some extent. The secretion of gastric acid is under control of the autonomic nervous system, but as with all other mechanisms of the gut, there is a close interaction between neuronal and local hormonal (endocrine and paracrine) signals to achieve a proper balance in the secretion of acid. In addition to the summary of the control of acid secretion, a short report on what little is known of the control of secretion of pepsinogen from the gut wall is included.

3.1. The oxynticopeptic cell

In most non-mammalian vertebrates, so called oxynticopeptic cells secrete both gastric acid and pepsinogen. This was originally determined by classical histochemical methods (Bishop and Odense, 1966; Mattisson and Holstein, 1980; Ezeasor, 1981; Garrido et al., 1993; Gallego-Huidobro and Pastor, 1996). A more recent study in winter flounder, *Pseudopleuronectes americanus*, using *in situ* hybridization with RNA probes for two pepsinogen genes and one proton pump gene (indicating the ability to secrete acid) confirms the occurrence of oxynticopeptic cells (Gawlicka et al., 2001). The cells are found in tubular gastric glands in the mucosa, most often in the anterior (cardiac or fundic) part of the stomach (Bishop and Odense,