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Research paper

Acetylsalicylic acid-induced changes in the chemical coding of extrinsic sensory neurons supplying the prepyloric area of the porcine stomach

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HIGHLIGHTS

- We found that 92% of the gastric sensory neurons originate in NGs while 8% in DRGs.
- The gastric sensory neurons within NGs express SP, CGRP, nNOS, VIP and GAL.
- The DRGs gastric neurons express SP, CGRP, nNOS, VIP and GAL.
- ASA-gastritis increased number of SP-, nNOS-, GAL-, VIP- as well as CGRP-IR neurons.
- These substances may evoke neuroprotective effects during inflammatory processes.

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ABSTRACT

Acetylsalicylic acid is a popular drug that is commonly used to treat fever and inflammation, but which can also negativity affect the mucosal layer of the stomach, although knowledge concerning its influence on gastric innervation is very scarce. Thus, the aim of the present study was to study the influence of prolonged acetylsalicylic acid supplementation on the extrinsic primary sensory neurons supplying the porcine stomach prepyloric region. Fast Blue (FB) was injected into the above-mentioned region of the stomach. Acetylsalicylic acid was then given orally to the experimental gilts from the seventh day after FB injection to the 27th day of the experiment. After euthanasia, the nodose ganglia (NG) and dorsal root ganglia (DRG) were collected. Sections of these ganglia were processed for routine double-labelling immunofluorescence technique for substance P (SP), calcitonine gene related peptide (CGRP), galanin (GAL), neuronal isoform of nitric oxide synthase (nNOS) and vasoactive intestinal polypeptide (VIP). Under physiological conditions within the nodose ganglia, the percentage of the FB-labeled neurons immunoreactive to particular substances ranged between 17.9 ± 2.7% (VIP-like immunoreactive (LI) neurons in the right NG) and 60.4 ± 1.7% (SP-LI cells within the left NG). Acetylsalicylic acid supplementation caused a considerable increase in the expression of all active substances studied within both left and right NG and the percentage of neurons positive to particular substances fluctuated from 47.2 ± 3.6% (GAL-LI neurons in the right NG) to 67.2 ± 2.0% (cells immunoreactive to SP in the left NG). All studied substances were also observed in DRG neurons supplying the prepyloric region of the stomach, but the number of immunoreactive neurons was too small to conduct a statistical analysis. The obtained results show that ASA may influence chemical coding of the sensory neurons supplying the porcine stomach, but the exact mechanisms of this action still remain unknown.

1. Introduction

Acetylsalicylic acid (ASA), also known as aspirin, is a very popular antipyretic, anti-inflammatory and analgesic drug, which has been known since the end of the 19th century [1]. The mechanism of action of ASA is based on inactivation of the cyclooxygenase (COX) enzyme, which takes part in the synthesis of prostaglandins, prostacyclin, as well as thromboxane A. It is known that there are three isoforms of cyclooxygenase: COX-1, which is present in the large number of cells in various tissues such as the mucosal layer of the digestive tract, kidneys, endothelium of blood vessels or thrombocytes; COX-2, which is induced by inflammatory processes and

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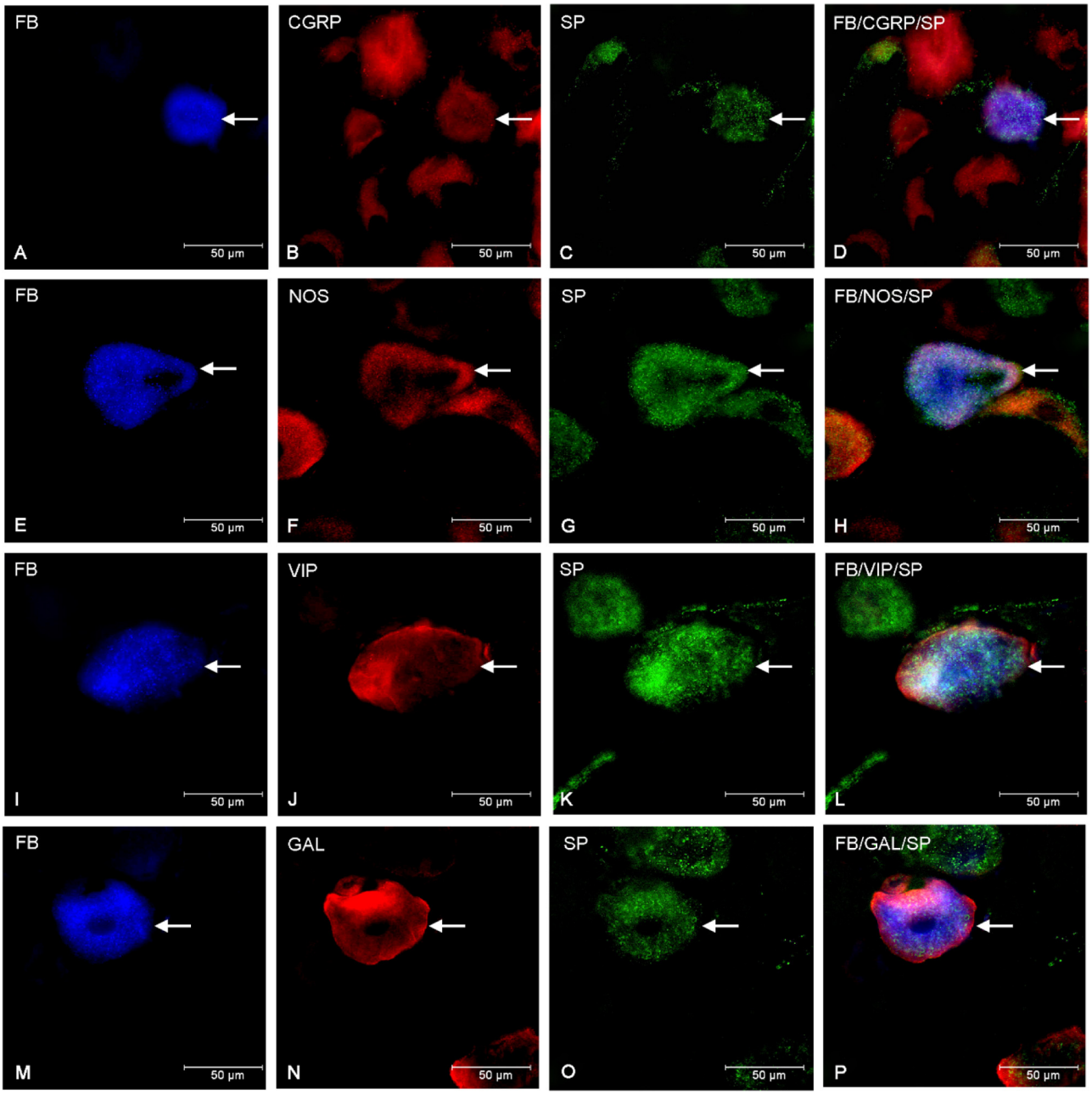

Fig. 1. Fluorescence photographs showing perikarya (arrows) immunoreactive to FB (A, E, I, M), SP (C, G, K, O); CGRP (B); NOS (F); GAL (J); VIP (N). (D) Shows double labelling FB/SP/CGRP (H)—FB/SP/NOS (L)—FB/SP/GAL (P)—FB/SP/VIP of the nodose ganglion neurons in control group.

COX-3 (variant of COX-1)—described in some species (dogs) within the central nervous system [1,2]. The action of aspirin, consisting of acetylation of the active site of above-mentioned enzyme, causes complete and irreversible inactivation of COX-1 and significant changes in the functioning of COX-2 [1,2]. Unfortunately, this action not only determines the widespread therapeutic use of ASA, but is also the cause of a wide range of undesirable actions of this drug, which are clearly visible especially within the stomach [3]. Previous studies show that even a single dose of aspirin may result in damage to the gastric mucosa. This damage is superficial and minor, but during long-term treatment with ASA, pathological changes in the gastric mucosa can increase due to a disturbance in mucus secretion, connected with inhibition of COX-1 [3,4].

Although the various mechanisms of action of ASA have become better known, the influence of this drug on the nervous system supplying the digestive tract still remains unclear [5]. The stomach, where the negative action of aspirin on the living organism is relatively well established [3], is innervated by both the enteric nervous system and extrinsic nerves. The former is located within the wall of the stomach and consists of two kinds of enteric ganglia: myenteric ganglia located between the longitudinal and circular muscle layers and submucous ganglia near the lamina propria of gastric mucosa [6,7]. Neurons supplying the stomach are also located within the vagal nuclei, dorsal root ganglia and celiac ganglia [5,8–11]. It is well-known that both the enteric nervous system as well as extrinsic innervation of the gastrointestinal tract are able to undergo structural, functional or chemical changes as a result of adaptive or reparative processes in response to physiological and pathological stimuli, such as development or aging, diet, drugs, nerve injury or intestinal and extra-intestinal diseases [12–14]. Contrary to intestinal enteric neurons, where the influences of various pathological stimuli on the expression of active substances are relatively