MORPHOFUNCTIONAL ALTERATIONS OF THE STOMACH IN AN EXPERIMENTAL MODEL OF CHRONIC STRESS

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ANNOTATION

Stress is an adaptive neuroendocrine response to factors that disturb homeostasis, and its chronic form is increasingly recognised as a driver of digestive pathology. The stomach is one of the most stress-sensitive organs, yet the dynamics of its structural and functional remodelling under experimental stress remain insufficiently described. The aim of this work is to characterise the morphofunctional changes of the rat stomach under continuous experimental stress. The study is performed on 120 white laboratory rats divided into control and experimental groups; stress is induced by keeping the animals in special labyrinth cages, and the material is examined on days 3, 7, 14, 21 and 30. Anatomical-topographic, organometric, histological (hematoxylin–eosin and Van Gieson staining), morphometric and biochemical methods are applied. The study is expected to provide new data on stress-related changes in gastric anatomy and mucosal morphology, forming a morphological basis for the prevention and early diagnosis of stress-associated gastric disorders.

Keywords: *experimental stress; chronic stress; stomach; gastric mucosa; morphofunctional changes; organometry; morphometry; laboratory rats.*

INTRODUCTION

Stress is an adaptive reaction of the organism, mediated by neurohormonal systems, to factors that disturb its internal balance [1, 2]. When intense or prolonged, it affects both mental and physical health, contributing to cardiovascular, metabolic and digestive disorders [2, 3]. The scale of the problem continues to grow: in 2024, 43% of adults in the United States reported feeling more anxious than in the previous year, compared with 37% in 2023 and 32% in 2022 [4], while across 31 countries an average of 62% of respondents stated that stress had affected their daily life at least once during the past year [5].

The digestive system, and the stomach in particular, is highly sensitive to stress. Activation of the hypothalamic–pituitary–adrenal axis and the sympathetic nervous system, largely through corticotropin-releasing factor, delays gastric emptying, alters motility and acid secretion and increases visceral sensitivity, which clinically manifests as epigastric pain, nausea and hyperacidity [3]. Stress also impairs blood flow in the gastric mucosa, weakening its protective barrier and raising the risk of inflammation and gastritis [3, 6], while chronic stress disturbs the gut microbiota, which in turn aggravates anxiety and depression through the gut–brain axis [7]. Since the COVID-19 pandemic, persistent gastrointestinal complaints (diarrhoea, bloating, abdominal pain) linked to psychological distress have also become more common [8].

The burden of digestive diseases also remains considerable. In 2019, digestive diseases accounted for 88.99 million disability-adjusted life years (DALYs) worldwide [9]. Gastric cancer ranked fifth in incidence, with 1,089,103 new cases and 768,793 deaths recorded in 2020 [10], and experimental data indicate that chronic stress may accelerate the progression of gastric precancerous lesions [11]. The complex aetiology, difficult treatment and high mortality of these diseases have drawn attention to the cellular composition of gastric regions, the role of endocrine cells and the interplay of vascular and nervous components. It is also known that morphological changes in the gastric wall may persist long after the causative factor has been eliminated. Although gastric morphology is well documented, its changes under experimental stress and their dynamics over time remain insufficiently studied.

The aim of the study is to investigate the morphofunctional changes of the stomach under experimental stress. **The objectives** are: (1) to identify changes in the anatomical and topographic structure of the stomach under experimental stress; (2) to study changes in the anatomical (organometric) parameters of the stomach under stress; (3) to provide a scientific substantiation of stress-induced changes in the morphological structure of the gastric mucosa.

MATERIALS AND METHODS

The experiment is carried out on 120 white laboratory rats divided into two groups. Group 1 (control) consists of healthy animals that receive 1.0 ml of physiological saline intragastrically every morning; a subclavian catheter is used as a gastric probe. Group 2 (experimental) includes 50 female rats kept in special labyrinth cages, in which the stress model is applied continuously throughout the experiment. The animals are euthanised under ether anaesthesia on days 3, 7, 14, 21 and 30, covering the early to late stages of stress.

After the abdominal cavity is opened, the anatomical and topographic position of the stomach and its relationship with the neighbouring organs are assessed, and the organ is removed. Its length, width and wall thickness are measured with a caliper, while the body weight of the animal and the weight of the stomach are determined with an electronic balance, allowing the relative weight of the organ to be calculated. Tissue samples from different parts of the stomach are fixed and embedded in paraffin; sections 8–10 μm thick are stained with hematoxylin and eosin and by the Van Gieson method. Morphometry includes measurement of the thickness of the mucosa and other layers of the gastric wall, the height of the surface epithelium and the depth of the gastric pits and glands. Biochemical methods complement the morphological assessment, and the data are processed by variation statistics (significance at $p < 0.05$).

RESULTS AND DISCUSSION

As the study is in progress, the expected results are outlined on the basis of the study design and published experimental data. In the early period of stress (days 3–7), acute vascular and mucosal reactions are anticipated: hyperaemia and oedema of the mucosa and submucosa, desquamation of the surface epithelium and focal erosions, predominantly in the glandular part of the stomach. These changes correspond to the alarm stage of Selye's general adaptation syndrome [1] and result from reduced mucosal blood flow, decreased mucus and bicarbonate secretion and increased aggressiveness of gastric juice [3].

As stress continues (days 14–21), a transition to adaptive and compensatory remodelling is expected: partial restoration of the epithelium, lymphocytic infiltration of the lamina propria and changes in mucosal thickness and gland height. This is consistent with experimental evidence that chronic restraint stress causes lymphocytic infiltration of the gastric mucosa, activation of oxidative stress and increased expression of pro-inflammatory cytokines (IL-1β, TNF-α), together with reduced activity of antioxidant enzymes [6].

By day 30, signs of exhaustion of adaptive mechanisms may appear: thinning of the mucosa, reduction of the glandular component and an increase in collagen fibres in the lamina propria and submucosa, which can be objectively assessed with Van Gieson staining. At the organ level, organometric indices (weight, length, width, wall thickness and relative weight of the stomach) are expected to change in parallel with the histological picture. Moreover, long-term stress may create a background for atrophic and dysplastic processes: in a rat model, chronic stress accelerated glandular atrophy and dysplasia and promoted angiogenesis in precancerous gastric lesions [11].

Comparing the experimental and control groups at each time point will make it possible to distinguish the stages of the gastric response to stress – damage, adaptation and exhaustion – and to determine the period during which morphological changes remain reversible. These data will complement current concepts of the gut–brain axis [3, 7] with objective morphological criteria.

CONCLUSION AND RECOMMENDATIONS

1. Stress is an important and growing risk factor for digestive disorders, and the stomach is one of its main target organs; however, the dynamics of gastric morphofunctional changes under experimental stress remain insufficiently studied.

2. The applied model (continuous stress in labyrinth cages with examination on days 3–30), combined with anatomical, organometric, histological, morphometric and biochemical methods, allows a comprehensive, stage-by-stage assessment of changes in the stomach and its mucosa.

3. The study will yield new data on the anatomical structure of the stomach under stress and provide a scientific substantiation of the morphological features of the gastric mucosa and their stress-related changes.

Recommendations. The results may be used in teaching human anatomy, histology and pathophysiology. In clinical practice, people exposed to chronic psycho-emotional stress should be regarded as a risk group for gastric pathology and considered for timely gastroenterological examination. Further studies should include immunohistochemical assessment of gastric endocrine cells and testing of gastroprotective interventions in the same model.

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