FUNCTIONAL AND METABOLIC REMODELING OF THE PANCREAS UNDER CHRONIC IMMOBILIZATION STRESS: EXPERIMENTAL EVIDENCE FROM RAT MODELS

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Abstract: *Chronic stress is increasingly recognized as a major contributor to metabolic disorders, endocrine dysfunction, and organ remodeling. The pancreas plays a central role in maintaining metabolic homeostasis through its endocrine and exocrine activities; however, its adaptive and maladaptive responses to prolonged stress remain insufficiently understood. This experimental study aimed to evaluate functional, biochemical, and metabolic alterations of the pancreas under chronic immobilization stress in rats. A total of 110 Wistar rats were subjected to immobilization stress, followed by assessment of glucose, insulin, C-peptide, HOMA-IR index, cortisol, adrenaline, and pancreatic enzymes (lipase, elastase, protease). The results demonstrated significant hyperglycemia, insulin resistance, activation of the hypothalamic–pituitary–adrenal axis, and dysregulation of digestive enzyme activity. These findings highlight the pancreas as a vulnerable target of stress-induced metabolic remodeling and emphasize the importance of early metabolic monitoring in chronic stress conditions.*

Keywords: *chronic stress, pancreas, insulin resistance, HOMA-IR, immobilization, metabolic adaptation.*

Introduction

Stress represents a universal biological response enabling organisms to adapt to environmental challenges. Acute stress responses are largely protective; however, persistent or chronic stress can disrupt metabolic homeostasis and promote pathological changes in endocrine organs. Epidemiological and experimental studies consistently link chronic stress with obesity, type 2 diabetes mellitus, cardiovascular disease, and inflammatory disorders.

The pancreas occupies a pivotal position in metabolic regulation by coordinating glucose homeostasis through insulin and glucagon secretion while simultaneously producing digestive enzymes essential for nutrient assimilation. Dysregulation of pancreatic function under stress may therefore amplify systemic metabolic disturbances.Activation of the sympathetic nervous system and the hypothalamic–pituitary–adrenal (HPA) axis increases circulating catecholamines and cortisol, enhancing gluconeogenesis, lipolysis, and protein catabolism. While these mechanisms ensure rapid energy availability during acute stress,

prolonged exposure induces insulin resistance, β-cell dysfunction, and altered exocrine secretion.

Despite extensive research on stress endocrinology, integrated assessment of endocrine and exocrine pancreatic responses under immobilization stress remains limited. The present study addresses this gap by providing a comprehensive biochemical evaluation of pancreatic adaptation to chronic stress.

Materials and Methods

Experimental Design

A total of 110 adult Wistar rats (Rattus norvegicus) were housed under standardized laboratory conditions. Animals were randomly divided into control and experimental groups. Chronic immobilization stress was induced daily using a standardized restraint protocol.

Biochemical Analysis

Blood samples were collected for determination of: Glucose,Insulin,C-peptide HOMA-IR index,Cortisol and adrenaline

Pancreatic enzymes: lipase, elastase, protease

Standard enzymatic and immunoassay methods were applied. Statistical analysis was performed using parametric methods with significance set at $p < 0.05$.

Results

Chronic immobilization stress induced pronounced metabolic alterations. Fasting glucose levels increased significantly compared with controls, accompanied by elevated insulin and C-peptide concentrations, indicating compensatory hyperinsulinemia.The HOMA-IR index showed a marked rise, confirming the development of insulin resistance. Cortisol and adrenaline levels were persistently elevated, reflecting sustained HPA axis activation.

Exocrine pancreatic activity demonstrated heterogeneous changes. Lipase and protease activities increased during early stress phases, suggesting adaptive hypersecretion, whereas prolonged exposure resulted in enzymatic instability and functional exhaustion.

Discussion. The findings confirm that chronic stress induces a metabolic shift toward insulin resistance and endocrine overload. Persistent hypercortisolemia disrupts insulin signaling and enhances hepatic glucose production. Catecholamines further amplify glucagon-mediated hyperglycemia.Exocrine enzyme dysregulation may reflect altered autonomic control and microcirculatory disturbances within pancreatic tissue. The parallel involvement of endocrine and exocrine compartments highlights the integrated vulnerability of the pancreas under chronic stress.These results provide mechanistic insight into stress-related metabolic syndrome development and suggest that pancreatic biomarkers may serve as early indicators of stress-induced pathology.

Conclusion. Chronic immobilization stress triggers significant endocrine and exocrine pancreatic remodeling, characterized by insulin resistance, hormonal imbalance, and enzymatic dysregulation. Early metabolic surveillance in stress-exposed populations may improve prevention of long-term metabolic disease.