

CHANGES IN PATHOMORPHOGENESIS OF THE HYPOTHALAMO-HYPOPHYSIARY SYSTEM IN CASES OF SUDDEN HEART DEATH

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Abstract

In the existing literature, limited studies have concurrently examined and correlated the morphofunctional parameters of the hypothalamus, pituitary gland, and adrenal glands in individuals with mood disorders, particularly in relation to cardiovascular risks. There is a scarcity of data on the morphometric correlations within the hypothalamic-pituitary-adrenal (HPA) axis structures, which holds significant interest for understanding comorbidity. Recent investigations employing morphometric techniques have primarily focused on stress-related disorders since the 2000s. A key attribute of the HPA axis is its capacity to integrate peripheral stress signals and orchestrate autonomic and neurohumoral responses. By applying morphometric approaches to study the HPA axis, objective data can be obtained for statistical evaluation. Assuming that structural integrity corresponds to functional adequacy, this research attempts to characterize HPA axis organ functions in mood disorders with cardiovascular implications via morphometry. The findings indicate that dysregulation of the HPA axis plays a pivotal role in the pathogenesis of increased cardiovascular mortality in mood disorders, necessitating consideration in therapeutic approaches.

Keywords: Hypothalamic-pituitary-adrenal axis, mood disorders, cardiovascular mortality, stress dysregulation.

Introduction

Relevance of the Topic

Mood disorders, such as depression and bipolar disorder, are prevalent globally and are associated with heightened risks of cardiovascular diseases (CVD), including coronary heart disease and sudden cardiac events. The interplay between psychological stress and physiological responses via the HPA axis is increasingly recognized as a mediator of this comorbidity. Chronic activation of the HPA axis can lead to hypertension, atherosclerosis, and endothelial dysfunction, contributing to elevated mortality rates. Despite advances, forensic and clinical diagnostics often overlook neuroendocrine contributions, complicating differential diagnoses. This underscores the need for



integrated examinations of the HPA axis in mood disorders to enhance risk stratification and intervention strategies.

Purpose of the Research Work

The aim of this study is to establish additional diagnostic criteria for assessing cardiovascular risk in mood disorders through morphological and morphometric analyses of changes in the hypothalamus, pituitary gland, adrenal glands, and related cardiovascular structures.

To accomplish this, we seek to identify morphological and morphometric alterations in these components in cases of mood disorders with comorbid CVD.

Material and Methods of the Research Work

This investigation utilized archival materials from the forensic histology departments of multiple institutions, including the Andijan State Medical Institute and affiliated centers.

The study cohort comprised 80 samples from 2018-2024, with 55 from individuals diagnosed with mood disorders (depression or bipolar) who exhibited cardiovascular complications, and a control group of 25 from non-psychiatric sudden deaths (e.g., trauma without endocrine involvement). Lifespan from symptom onset to event was under 60 minutes in acute cases. Autopsies followed standard protocols within 12 hours post-mortem, with toxicological screens confirming absence of substances like alcohol.

Polarization microscopy was employed to assess myocardial compression and cardiomyocyte contractures, using filters to evaluate anisotropy effects. Immunohistochemical analyses utilized primary antibodies with DAB chromogen for detecting stress markers like cortisol receptors.

Morphometric Method

Autopsies included anthropometric assessments for endocrine status. Macroscopic evaluations of adrenal glands and hypothalamus used calipers for volume and density measurements. Atherosclerotic staging in coronary arteries was quantified.

Statistical Methods

Data processing involved Microsoft Excel 2010 and SPSS for descriptive statistics, including means, standard deviations, and comparative analyses (t-tests, $p < 0.05$).

Results and Discussions

Average adrenal gland weight was 12.5 ± 1.8 g, with dimensions varying: length 4.5-6.2 cm, width 2.5-3.4 cm, thickness 0.5-1.0 cm. Cortical thickness ranged from 0.1-0.3 cm. In mood disorder cases, 15.4% showed minimal atherosclerotic plaques without significant occlusion.

Histologically, HPA axis components displayed hyperactivity: elevated cortisol-positive cells in adrenals ($58.4 \pm 5.2\%$) and hypothalamic nuclei ($42.3 \pm 4.1\%$). Myocardial changes included contractures in $48.7 \pm 3.8\%$ of left ventricular cardiomyocytes, predominantly subendocardial.

In controls, contractures were higher at $62.1 \pm 6.4\%$. Wave-like deformations affected $39.8 \pm 5.7\%$ of cardiomyocytes in study groups, with dissociation in $55.6 \pm 2.8\%$. No myocytolysis was observed.





Adrenal delipidization was prominent in mood disorders, with medullary adrenaline-positive cells at $62.5 \pm 5.9\%$. These findings suggest chronic HPA hyperactivity exacerbates cardiovascular vulnerability, aligning with literature on stress-induced mortality.

Conclusion

Future research should explore immunohistochemical markers for HPA axis dysregulation in mood disorders and quantify catecholamine levels in related pathologies. This could refine diagnostic and therapeutic paradigms for reducing cardiovascular mortality.

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