

European Endocrinology and **DIABETES CONGRESS**

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Endocrine Factors in Key Structural and Intracellular Changes in Depression**Philip Gold***Duke University School of Medicine*

The World Health Organization Ranks depression as the 2nd greatest cause of disability worldwide, and the greatest cause of disability in individuals under the age of forty. In addition to its affective and cognitive components, depression is associated with the premature onset of coronary artery disease, diabetes, stroke, and osteoporosis. Overall, patients with depressive illness have a lifespan shortened by approximately seven years.

Multiple lines of evidence indicate that depression represents a stress system that has run awry. There are two principle clinical subtypes of depression that I will demonstrate reflect different perturbations in stress system function, melancholic and atypical depression. Melancholic depression contradicts the term depression in that it is often a state of hyperarousal, anxiety, anguished feelings of worthlessness, insomnia, and anorexia. Patients have increased secretion of corticotropin releasing hormone (CRH), cortisol, and norepinephrine, they often manifest pathological inflammation, and their symptoms are more severe in the morning, when the stress system is most active. Atypical depression seems the antithesis of melancholic depression and is associated with decreased activity of the CRH system, hypersomnia, hyperphagia, and profound fatigue. Symptoms are at their worst in the evening, when the stress system is near its nadir. Overall, melancholia appears to be a pathological activation of the stress response, while atypical depression seems like a pathological inactivation of the stress system.

Endocrine disturbances play predominant roles in recently discovered, clinically-relevant abnormalities in depression. These affect multiple sites in the prefrontal cortex, amygdala, hippocampus, nucleus accumbens, and habenula. Deficits consist of changes in volume, neuroplasticity, neural connectivity, synapse composition, and neurogenesis. Depression is associated with endocrine-related, premature systemic disease, that result in a loss of approximately seven years of life. In addition to CRH, glucocorticoids, somatostatin, gonadal steroids, and thyroid hormones all contribute to the anatomic and functional deficits that largely define the pathophysiologic presentation of depression.

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