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Article Review: Neuroendocrine Interplay: How Hormones Shape Human Psychology and Mental Disorders

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Annotation: This article examines the critical link between hormones and psychological states, essential for understanding mental health and behavior. It notes that aggressive behavior in psychiatric patients may stem from hormonal imbalances and surveys prevalent mental disorders worldwide—including anxiety disorders (excessive fear), depression (persistent low mood), bipolar disorder (extreme mood swings), PTSD (post-trauma effects), and schizophrenia (disrupted cognition and behavior), alongside eating and behavioral disorders. Affecting millions globally, these conditions highlight the need to explore their biological and psychological underpinnings.

Hormones, defined as chemical messengers from endocrine glands, regulate bodily functions via the bloodstream. Beyond simple signaling, they intricately modulate growth, metabolism, homeostasis, mood, and emotions. Key hormones influencing mental health include: serotonin (mood and anxiety regulation), cortisol (stress response), dopamine (reward and motivation), oxytocin (social bonding), melatonin (sleep cycles), and ghrelin/leptin (appetite control). Imbalances in these systems can trigger mental health disorders.

The article underscores that deciphering hormone-psychology interactions is vital for

advancing mental health treatments and improving well-being.

Keywords: psychology, hormone, neuroendocrine.

Introduction

Aggressive behavior is prevalent among psychiatric patients, manifesting as either hetero-aggression (toward others) or auto-aggression (self-harm), often stemming from impaired impulse control. This poses significant public health risks, as it contributes to criminal offenses. Aggression and suicidal behavior share neurobiological underpinnings [1], with causes ranging from auditory hallucinations (e.g., in schizophrenia) to disinhibition (e.g., bipolar disorder) or personality disorders.

This review explores hormonal influences on aggression in mental health disorders. The interplay between the central nervous and endocrine systems regulates homeostasis and stress responses—an evolutionarily conserved mechanism governing human-environment interactions. Psychiatric disorders often disrupt hormonal balance (due to the disease or medications), while endocrine dysfunctions can trigger psychiatric symptoms [2].

Global mental health statistics (2019) highlight the burden of these conditions:

- ✓ Anxiety disorders: 301 million cases (57 million children/adolescents) [3]
- ✓ Depression: 170 million (23 million children/adolescents), with high suicide risk [3]
- ✓ Bipolar disorder: 25 million, featuring mood swings and suicide risk [3]
- ✓ PTSD: Elevated prevalence in conflict zones [4]
- ✓ Schizophrenia: 24 million, with reduced life expectancy [5]
- ✓ Eating disorders: 14 million (3 million children/adolescents) [3]
- ✓ Behavioral disorders: 25 million, including conduct disorders [3]

Neurodevelopmental disorders (e.g., autism, ADHD) further compound this burden. While treatments exist, this study focuses on how hormonal and neurotransmitter imbalances (e.g., serotonin, cortisol, dopamine) contribute to these conditions, informing targeted interventions.

Hormones:

The Body's Master Regulators

Hormones are chemical messengers produced by endocrine glands that travel through the bloodstream to regulate physiological processes. Far from simple signals, they form a complex communication network—like the body's internal internet—coordinating growth, metabolism, reproduction, and homeostasis from conception through aging.

Key Functions:

- ✓ Development: Govern growth, puberty, and sexual maturation
- ✓ Metabolism: Regulate energy use/storage (e.g., insulin, glucagon) [6]
- ✓ Homeostasis: Maintain stable internal conditions (blood sugar, electrolytes)
- ✓ Emotion/Motivation: Influence mood, stress responses (e.g., adrenaline surges)

System Dynamics:

The endocrine system (thyroid, adrenal, pituitary, etc.) releases hormones in precise feedback

loops, often with:

- Multi-hormone coordination: Multiple hormones (e.g., cortisol, growth hormone) may regulate one process like metabolism [6]
- Pleiotropic effects: Single hormones (e.g., cortisol) can impact multiple organs [7]

Clinical Relevance:

Hormonal imbalances underlie disorders like diabetes, infertility, and mood disorders. Their interplay with the nervous system [6] is vital for both cellular function and emergency responses. Understanding this network enables targeted treatments to restore balance and health.

Hormones are categorized into three primary chemical classes based on structure and function:

1. Steroid Hormones

✓ Derived from cholesterol

✓ Lipid-soluble (e.g., cortisol, testosterone)

2. Peptide/Protein Hormones

✓ Chains of amino acids

✓ Water-soluble (e.g., insulin, growth hormone)

3. Amine Hormones

✓ Derived from single amino acids (e.g., thyroid hormones, epinephrine)

Hormones that have an effect on the psychological state of a person

Serotonin

Serotonin (5-HT) is a crucial neurotransmitter regulating mood, behavior, memory, and gut function[8]. Produced in the brainstem's raphe nuclei and intestinal cells [9], its dysfunction links to depression, PTSD, OCD, and anxiety [10]. While other neurotransmitters (e.g., dopamine) are treatment targets, serotonin-focused therapies (SSRIs/SNRIs) remain first-line, combined with lifestyle and psychotherapy [11].

Mechanism of Action

Released into synapses, serotonin binds to 5-HT receptors (GPCRs/ionotropic) in the CNS/PNS, modulating excitatory/inhibitory signals [12].

Functions

- CNS: Governs mood, sleep, appetite, stress, and pain [13]. Low serotonin underpins depression (affecting 20% globally [14]), treated with SSRIs/SNRIs that boost synaptic serotonin/noradrenaline [15].

Low Serotonin Effects

Linked to:

✓ Mood disorders (depression, anxiety)

✓ Sleep/digestive issues

✓ OCD, PTSD, schizophrenia, suicidal behavior

Causes of Deficiency

✓ Inadequate production

✓ Dysfunctional receptors

Serotonin Syndrome (SS)

Excess serotonin causes life-threatening symptoms:

- ✓ Neuromuscular: Tremors, hypertonia
- ✓ Autonomic: Fever, tachycardia, vomiting
- ✓ Neurological: Agitation, confusion [16].

Cortisol Hormone

Cortisol Hormone

Cortisol is commonly known as the body's primary stress hormone, but it plays a much broader role in regulating various physiological functions. Produced in the zona fasciculata of the adrenal cortex, its secretion is tightly controlled by the hypothalamic-pituitary-adrenal (HPA) axis. When this regulatory system malfunctions, it can lead to either excessive cortisol levels, as seen in Cushing's syndrome, or insufficient production, as in Addison's disease.

Mechanism of Action

Cortisol release is governed by the HPA axis, which begins with the hypothalamus secreting corticotropin-releasing hormone (CRH) [2]. This hormone stimulates the anterior pituitary gland to release adrenocorticotropic hormone (ACTH), which then signals the adrenal cortex to produce cortisol. Elevated cortisol levels subsequently inhibit further CRH and ACTH secretion through a negative feedback loop, maintaining balance.

As a steroid hormone, cortisol is lipid-soluble, allowing it to easily pass through cell membranes. Inside the cell, it binds to glucocorticoid receptors (GR) in the cytoplasm. In their inactive state, these receptors are bound to Hsp90 chaperone proteins. Cortisol binding triggers the dissociation of Hsp90, enabling the cortisol-receptor complex to enter the nucleus and modulate gene expression [16].

Cortisol Receptors

The body expresses two primary intracellular receptors for cortisol: glucocorticoid receptors (GR) and mineralocorticoid receptors (MR). GRs are nearly ubiquitous, found in almost all tissues, while MRs are more localized, primarily present in the brain, kidneys, colon, heart, and sweat glands [17]. Due to the widespread distribution of these receptors, cortisol exerts influence over multiple organ systems, including the nervous, immune, cardiovascular, respiratory, reproductive, musculoskeletal, and integumentary systems [18].

Normal Cortisol Levels

Cortisol secretion follows a distinct circadian rhythm, with levels peaking in the early morning (typically between 6-7 a.m., ranging from 10 to 20 mcg/dL) and gradually declining throughout the day, reaching their lowest point around midnight. This pattern can be disrupted in individuals with irregular sleep schedules, such as night shift workers. Normal ranges may vary slightly depending on the laboratory and individual factors. If testing is required, healthcare providers can interpret results and determine whether further evaluation is necessary.

Effects of High Cortisol on Psychological Well-Being

Chronically elevated cortisol levels are strongly associated with increased anxiety and stress, often leading to irritability and heightened emotional reactivity. Additionally, prolonged exposure to high cortisol may contribute to the development or exacerbation of depressive symptoms, though the relationship between cortisol and depression is complex and multifaceted.

Effects of Low Cortisol on Psychological Well-Being

Insufficient cortisol production can result in persistent fatigue and a profound lack of energy,

significantly impacting daily functioning and overall mood. Low cortisol levels have also been linked to an increased risk of depression, with symptoms such as sadness, loss of interest, and low motivation. While anxiety is more commonly associated with high cortisol, some individuals with low cortisol may experience heightened irritability or anxiety-like symptoms.

Cognitive functions, including concentration and attention, may also be impaired. Additionally, individuals with low cortisol often struggle to cope with stress, as the hormone plays a critical role in the body's stress response. Over time, this can lead to emotional instability, mood swings, and even apathy, characterized by a diminished interest in previously enjoyable activities.

Dopamine hormone

Dopamine (DA) is crucial for reward processing and motor control. In the reward pathway, DA is produced in the ventral tegmental area (VTA) and released into the nucleus accumbens and prefrontal cortex. In vivo concentrations are 4.7 ± 1.5 nM (VTA) and 0.5 ± 1.5 nM in red nucleus[19].

For movement regulation, DA is synthesized in the substantia nigra and transmitted to the striatum. Beyond motor and reward functions, DA influences cognition, motivation, mood, sleep, learning, and prolactin inhibition[20].

DA is also a precursor for norepinephrine (NE) and epinephrine:[21]

- ✓ NE forms via dopamine β-hydroxylase (using O_2 and vitamin C).
- ✓ Epinephrine is produced from NE via PNMT (with SAMe as a cofactor).

After synthesis, DA is stored in synaptic vesicles (via VMAT2) and released via exocytosis. Dysregulation in DA pathways is linked to neurological and psychiatric disorders, making tyrosine hydroxylase (TH) regulation a potential therapeutic target[22].

Dopamine receptors

Dopamine (DA) receptors in the synapse can be postsynaptic or presynaptic. Binding to either triggers an electric potential in the presynaptic cell [22].

- ✓ Postsynaptic receptors propagate signals to the postsynaptic neuron.
- ✓ Presynaptic receptors (autoreceptors) can excite or inhibit the presynaptic cell. Inhibitory autoreceptors regulate DA levels by suppressing synthesis and release [22].

After synaptic action, DA is reuptaken via:

1. High-affinity DAT or low-affinity monoamine transporters.
2. Amphetamine reverses DAT, ejecting DA from vesicles into the synapse [23].
3. DAT (Na^+-coupled symporter) controls extracellular DA levels [24].

Repackaging into vesicles is mediated by VMAT2 [25].

Mechanism of Action

Dopamine (DA) synthesis begins with **tyrosine** in dopaminergic neurons, sequentially converted to:

1. **L-DOPA** via *tyrosine hydroxylase*
2. **Dopamine** via *aromatic L-amino acid decarboxylase*

Stored in synaptic vesicles until neuronal firing triggers release into the synaptic cleft.

Receptor Signaling

DA binds to two G protein-coupled receptor families:

- D1-like (D1/D5): ↑ *Adenylyl cyclase* → ↑ cAMP → *PKA activation* → Alters gene expression/neurotransmitter release.
- D2-like (D2-D4): ↓ *Adenylyl cyclase* → ↓ cAMP → *Reduced PKA activity* → Inhibits neuronal excitability/release.

Termination of Signal

1. Reuptake via *dopamine transporter (DAT)* into presynaptic neuron.
2. Repackaged into vesicles or degraded by *MAO/COMT* enzymes.

Dopamine functions

Dopamine serves as the brain's primary reward neurotransmitter, reinforcing essential behaviors like eating and social interaction [26]. It functions as both a pleasure signal ("liking") and motivational driver ("wanting"), with these components dissociating in addiction - craving increases while pleasure decreases [27].

The dopamine system encodes reward prediction error, firing strongly to unexpected rewards but showing no response to predicted ones or dips when rewards are omitted [28]. This precise signaling aligns with computational learning models, particularly temporal difference learning, creating important intersections between neuroscience and machine learning [29].

Other function of dopamine

Dopamine has diverse roles including: motor control (substantia nigra production, Parkinson's link); mood regulation (depression/bipolar connections); cognitive functions (prefrontal cortex activity); motivation; prolactin inhibition; and learning/memory reinforcement through neural pathway strengthening.

Dopamine levels

What happens if I have too much or too little dopamine?

Dopamine imbalances in specific brain regions are associated with various mental health conditions. Excessive dopamine activity has been linked to aggression, impulse control difficulties, and conditions like schizophrenia, psychosis, and ADHD. Conversely, dopamine deficiency contributes to Parkinson's disease (characterized by movement impairments) and symptoms like reduced motivation, fatigue, and depression. Physical manifestations may include muscle rigidity, digestive issues, respiratory infections, and slowed movement or speech. Psychological effects range from low mood and decreased libido to severe perceptual disturbances like hallucinations. These symptoms reflect dopamine's crucial role in regulating movement, motivation, emotional states, and cognitive processing.

Oxytocin

Oxytocin: The "Love Hormone"

Oxytocin is a peptide hormone and neuropeptide synthesized in the hypothalamus and secreted by the posterior pituitary [30]. Evolutionarily conserved, it influences social bonding, reproduction, childbirth, and postpartum processes (31,32). It is released during sexual activity, labor, and breastfeeding [33].

Physiological Roles

- Childbirth: Stimulates uterine contractions via a positive feedback loop, intensifying labor [34].
- Lactation: Promotes milk ejection and maternal bonding [34,35].

- Mechanism: Binds to uterine oxytocin receptors, increasing intracellular calcium to enhance contractions [36].

Psychological & Behavioral Effects

Oxytocin acts on brain regions like the amygdala and prefrontal cortex, modulating social behavior and emotional responses.

Oxytocin in Psychiatric Disorders

Recent studies suggest oxytocin as a potential biomarker for mental health conditions [42]:

- Reduced levels are linked to:
- ✓ Schizophrenia (inversely correlated with negative symptoms)
- ✓ Autism spectrum disorder (ASD) (associated with impaired social skills)
- ✓ Depression, PTSD, and anxiety disorders [43,39].
- Oxytocin receptor polymorphisms (e.g., rs5265, rs2252687) may influence susceptibility to mood and personality disorders [40].

Therapeutic Applications

Intranasal oxytocin is being explored for its prosocial effects and tolerability [41]. Potential uses include:

- ✓ Schizophrenia
- ✓ Mood disorders (e.g., MDD, bipolar disorder)
- ✓ ASD (improving social cognition)
- ✓ PTSD and anxiety disorders
- ✓ Substance use and eating disorders

Abnormal Oxytocin Levels

- Low levels: Rare but associated with panhypopituitarism, impaired labor, and lactation. Linked to ASD and depression (research ongoing) [42,43].
- High levels (oxytocin toxicity):
- ✓ Females: Uterine hypertrophy, pregnancy complications.
- ✓ Males: Benign prostatic hyperplasia (BPH), affecting urination (common in men >36).

In conclusion, Oxytocin regulates physical and emotional bonding, with emerging roles in mental health treatment. Further research is needed to clarify its therapeutic potential.

Endorphins

Endorphins: The Body’s Natural Pain and Pleasure System

Introduction and Basic Function

Endorphins are endogenous opioid peptides produced primarily in the hypothalamus and pituitary gland [42]. These neurochemicals function as the body's natural pain relievers and mood enhancers by binding to opioid receptors throughout the nervous system [43].

Mechanism of Action

Endorphins exert their effects through:

1. Pain modulation by inhibiting substance P release at nerve endings
2. Pleasure enhancement via dopamine release in reward pathways

3. Stress regulation through interactions with the HPA axis

Role in Psychiatric Disorders

Research demonstrates complex relationships between endorphins and mental health:

- Depression: Studies show mixed results, with both elevated and reduced β-endorphin levels reported [44]
- PTSD: Consistently associated with lower endorphin levels and impaired stress response [45,46]
- Chronic pain conditions: Often correlate with endorphin dysregulation

Clinical Implications

Endorphin deficiency may manifest as:

- ✓ Increased pain sensitivity
- ✓ Mood disturbances (depression/anxiety)
- ✓ Addictive behaviors (substance abuse, exercise addiction)

Therapeutic Potential

Current evidence suggests:

- ✓ Exercise moderately increases endorphin levels
- ✓ The endorphin system represents a potential target for novel antidepressants
- ✓ More research is needed to clarify central vs. peripheral effects

In conclusion, while endorphins clearly play important roles in pain and emotional processing, their precise involvement in psychiatric disorders requires further investigation. The complexity of their actions in different body compartments and disease states presents both challenges and opportunities for therapeutic development.

Melatonin

Melatonin: The Sleep-Regulating Hormone

Overview and Production

Melatonin is a neurohormone primarily secreted by the pineal gland (6.2 mm in humans) in response to darkness. It regulates circadian rhythms in humans and seasonal behaviors in animals. Production follows a light-dependent pathway: retinal detection of darkness triggers norepinephrine release, converting serotonin to melatonin via AANAT and ASMT enzymes.

Mechanisms of Action

Melatonin exerts effects through:

- Receptor-dependent pathways:
- ✓ MT1 receptors (inhibit cAMP)
- ✓ MT2 receptors (regulate calcium)
- Receptor-independent actions:
- ✓ Potent antioxidant activity
- ✓ Direct free radical scavenging

Key physiological roles include:

- ✓ Core body temperature reduction

- ✓ Neurotransmitter modulation (serotonin/dopamine)
- ✓ BDNF-mediated neuroplasticity enhancement
- ✓ Transgenerational rhythm programming (placental transfer)

Clinical Relevance in Depression

Circadian disruption is implicated in depression pathogenesis [47]. Evidence suggests:

- ✓ 6-sulfatoxymelatonin (aMT6s) may predict antidepressant response [49,50]
- ✓ Animal models show antidepressant-like effects [51-53]
- ✓ Human trials remain inconclusive [54,55]

Therapeutic Use

Approved applications:

- ✓ Circadian rhythm disorders (0.5-5 mg doses)
- ✓ Delayed sleep phase syndrome
- ✓ Jet lag management [56,57]

Levels and Supplementation

Normal daily production: ~30 μg (70% nocturnal)

- ✓ Daytime plasma: 10-20 pg/mL
- ✓ Nighttime peak: 70-56 pg/mL

Abnormal Levels:

- ✓ Deficiency: Linked to insomnia, aging, and stress
- ✓ Excess: May cause drowsiness, headaches (rarely tumors)

Supplementation Guidelines:

- ✓ Typical dose: 0.5-5 mg
- ✓ Timing: 1-2 hours before bedtime

Conclusion

While melatonin clearly regulates sleep/circadian function, its antidepressant potential requires further study. Current evidence supports its use primarily for circadian-related sleep disorders. The dual receptor-dependent and antioxidant mechanisms make it unique among neurohormones.

Ghrelin

Ghrelin: The Hunger Hormone with Neuropsychological Roles

Overview and Production

Ghrelin is a 17-amino acid peptide hormone primarily produced by:

- ✓ P/D1 cells in gastric fundus
- ✓ Pancreatic epsilon cells [58]

Unique as the only known orexigenic (appetite-stimulating) gut hormone, its secretion increases during fasting and decreases postprandially [59].

Mechanism of Action

Ghrelin exerts effects through:

1. Central nervous system binding:

✓ Activates GHSR1a receptors in hypothalamus (arcuate nucleus)

✓ Stimulates NPY/AgRP neurons while inhibiting POMC neurons [60,61]

2. Peripheral actions:

✓ Enhances gastric motility and acid secretion

✓ Stimulates growth hormone release [60]

Neuropsychological Functions

Emerging research reveals ghrelin's roles in:

✓ Hippocampal neuroprotection and cognitive adaptation [62]

✓ Mood regulation via dopaminergic reward pathways

✓ Stress response modulation through HPA axis interaction [63]

Clinical Associations with Mental Health

Research shows complex relationships:

Depression:

✓ Elevated levels reported in some MDD patients [64]

✓ Potential antidepressant effects in male MDD patients [65]

✓ Contrasting studies show no difference or reduced levels [66,67]

Anxiety:

✓ Animal studies show both anxiogenic and anxiolytic effects [68,57]

✓ Human data suggests stress-induced elevation [69]

Therapeutic Implications

Key findings include:

✓ Fasting-induced ghrelin may improve mood via dopamine

✓ Chronic stress may dysregulate ghrelin signaling

✓ Potential biomarker for treatment response [67]

Pathological Conditions

Elevated Ghrelin:

✓ May protect against stress-induced anxiety

✓ Could increase PTSD vulnerability

✓ Associated with hyperphagia and weight gain

Reduced Ghrelin:

✓ Linked to increased anxiety symptoms

✓ May impair stress adaptation

✓ Associated with metabolic dysfunction

In conclusion Ghrelin's dual role in appetite regulation and neuropsychological function makes it unique among gut hormones. While evidence suggests involvement in mood and stress disorders, the exact mechanisms remain unclear. Further research is needed to clarify its potential as a therapeutic target in psychiatric conditions.

Leptin

Leptin: The Satiety Hormone with Neuroendocrine Roles

Overview & Production

Leptin is a protein hormone primarily secreted by white adipose tissue, playing a key role in:

- ✓ Appetite suppression (via hypothalamic signaling)
- ✓ Energy expenditure & metabolism
- ✓ Immune & reproductive function [70]

Mechanism of Action

Leptin binds to Ob-R receptors in the hypothalamus, regulating:

1. Appetite control:
- ✓ Inhibits NPY/AgRP (hunger-stimulating neurons)
- ✓ Activates POMC/CART (satiety-promoting neurons)
2. Metabolic effects:
- ✓ Stimulates thermogenesis (brown fat activation)
- ✓ Reduces lipogenesis (fat storage)
3. Neuroendocrine roles:
- ✓ Modulates GnRH (reproductive hormones)
- ✓ Influences bone density (osteoblast/osteoclast activity) [71]

Leptin in Mood Disorders

Studies show conflicting associations between leptin and mental health:

- ➢ Depression:
- ✓ Low leptin linked to MDD, suicide attempts (independent of BMI) [72]
- ✓ High leptin observed in atypical depression & inflammation-related cases [73]
- ➢ Anxiety:
- ✓ Low leptin correlates with higher anxiety (possibly due to HPA axis dysregulation) [72]
- ➢ Antidepressant effects:
- ✓ Some SSRIs increase leptin, suggesting a role in treatment response [74]

Clinical Implications

Normal Leptin Levels:

- ✓ Women: 0.5–15.2 ng/mL
- ✓ Men: 0.5–12.5 ng/mL

High Leptin (Leptin Resistance):

- ➢ Associated with:
- ✓ Obesity & metabolic syndrome

- ✓ Depression/anxiety (via inflammatory pathways)
- ✓ Reward system dysfunction (food addiction risk)

Low Leptin:

- ➢ Linked to:
- ✓ Increased depression risk (low CSF leptin in suicidal patients) [75]
- ✓ Anxiety & irritability (e.g., anorexia nervosa)
- ✓ HPA axis hyperactivity (chronic stress susceptibility)

In conclusion Leptin's dual role in metabolism and neuropsychiatry highlights its importance in both physical and mental health. While low leptin may contribute to mood disorders via neurotransmitter disruption, high leptin (often with resistance) is tied to obesity-related inflammation and reward dysfunction.

Thyroid Hormones

Thyroid hormones, produced by the thyroid gland, include triiodothyronine (T3) and thyroxine (T4). Derived from tyrosine, they regulate metabolism and contain iodine. Iodine deficiency reduces T3/T4 production, causing goiter (thyroid enlargement) [76].

T4 is the primary circulating hormone, with a longer half-life than T3. The blood T4:T3 ratio is ~14:1. T4 converts to active T3 (3–4x more potent) via 5′-deiodinase (a selenium-dependent enzyme), emphasizing the need for dietary selenium [77]. T4 also metabolizes into iodothyronamine (T1a) and thyronamine (T0a).

Mechanism of Thyroid Hormone Action

T4 and T3 act via a hypothalamus-pituitary-thyroid (HPT) axis:

1. Hypothalamus releases thyrotropin-releasing hormone (TRH).
2. Pituitary secretes thyroid-stimulating hormone (TSH).
3. Thyroid produces T4/T3, which bind to blood carrier proteins.

Cellular Effects:

- ✓ T3 enters cells, binding nuclear receptors to modulate gene expression.
- ✓ Increases basal metabolic rate (oxygen use, heat production).
- ✓ Regulates growth, cardiovascular function, nervous system activity, digestion, and muscle function.

Feedback Loop: High T3/T4 inhibits TRH/TSH, maintaining hormonal balance.

Functions of Thyroid Hormones

Link to Depression

- ➢ Hypothyroidism and depression share overlapping symptoms (e.g., lethargy, cognitive decline).
- ➢ Thyroid hormones influence noradrenergic/serotonergic pathways (targets of antidepressants) [77].
- ➢ Neuropsychiatric symptoms include depression, apathy, psychosis, and cognitive impairment [78].

Historical & Clinical Evidence:

- ✓ 657: First link between hypothyroidism and psychosis [79].

- ✓ 1930: "Myxedema madness" described severe hypothyroidism with psychosis [80].
- ✓ 31% of treatment-resistant depression cases involve subclinical hypothyroidism [80].
- ✓ 20% of depressed patients have antithyroid antibodies [77].
- ✓ Severe cases may include suicidal thoughts, delusions, or hallucinations. Mania is rare but possible in hypothyroidism [77].

Thyroid Hormone Imbalances

1. Hyperthyroidism (High Hormones)

- ➢ Causes: Graves' disease, thyroid nodules, thyroiditis.

2. Hypothyroidism (Low Hormones)

- ➢ Cause: Hashimoto's disease.

Estrogen and Progesterone Hormones

Estrogens[81] are female sex hormones primarily secreted by the ovaries. Derived from fatty esters or linked to estrus (the ovulation period), they are steroid hormones in vertebrates[82] and some insects,[83] indicating an ancient evolutionary origin. Natural estrogens are steroids, while some synthetic versions are non-steroidal. The term "estrogen" combines Greek words for "sexual appetite" (estrus/οίστρος) and "to generate" (gen/γόνο). Estrogen production declines at menopause,[84] leading to risks like osteoporosis.

Progesterone, a steroid hormone, is secreted by the ovarian corpus luteum during the luteal phase (last two weeks of the menstrual cycle). It is also produced by the adrenal cortex in both sexes and by the placenta during pregnancy, peaking near birth. Progesterone thickens the uterine lining to support embryo implantation.

Mechanism of Action of Estrogen and Progesterone

Estrogen, produced mainly in the ovaries, regulates the menstrual cycle by stimulating endometrial growth and influences secondary sexual characteristics, mood, bone health, and ovulation. Progesterone, secreted by the corpus luteum and placenta, prepares the endometrium for pregnancy, prevents uterine contractions, and stabilizes mood.

During the menstrual cycle, estrogen rises first to thicken the endometrium. Post-ovulation, progesterone increases to support potential implantation. If pregnancy doesn't occur, progesterone drops, triggering menstruation. In pregnancy, progesterone sustains the endometrium and prevents contractions.

Functions of Estrogen and Progesterone

Estrogen profoundly affects mood, memory, and cognition. Its cyclical fluctuations can cause premenstrual mood swings or menopausal anxiety/depression. It also enhances brain cell function, with declines linked to memory and concentration issues.

Progesterone imbalances may contribute to PMS and postpartum depression. Its sedative effects and impact on brain metabolism may explain mood changes, though mechanisms remain speculative. Contraceptives containing progesterone may help severe premenstrual dysphoria but require further study.[85]

Normal Estrogen Levels

Estrogen fluctuates naturally (e.g., rising during puberty/ovulation, falling during menstruation/menopause). Consistently low or high levels may indicate underlying conditions.

Low Estrogen Symptoms:

- ✓ Hot flashes, night sweats

- ✓ Irregular/no periods, vaginal dryness
- ✓ Mood swings, fatigue, weak bones

High Estrogen Symptoms:

- ✓ Weight gain, irregular bleeding
- ✓ Decreased libido, worsened PMS

Normal Progesterone Levels

Progesterone levels vary by menstrual phase and pregnancy. Healthcare providers assess levels based on cycle timing or pregnancy status.

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