Νευροφυσιολογία και Αισθήσεις

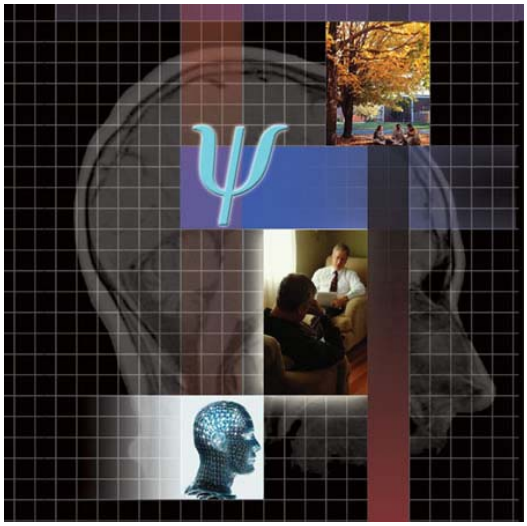
Διάλεξη 19

Ψυχασθένειες

(Mental Illness)

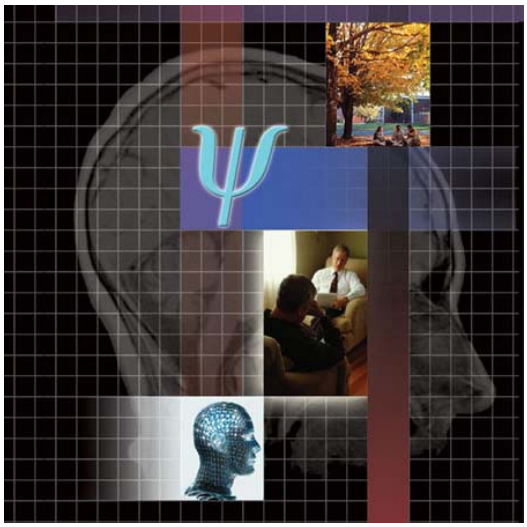
Introduction

- **Neurology**
  - Branch of medicine concerned with the diagnosis and treatment of nervous system disorders
- **Neurological disorders**
  - Help illustrate the role of physiological processes in normal brain function
- **Psychiatry**
  - Branch of medicine concerned with the diagnosis and treatment of disorders that affect the mind or psyche
- **Psychiatric disorders**
  - Examples: Anxiety disorders, affective disorders, schizophrenia



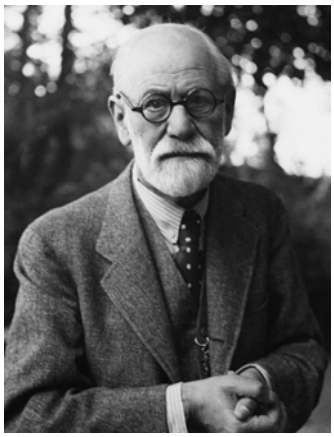
Mental Illness and the Brain

- **Mental illness**
  - Diagnosable disorder of thought, mood, or behavior that causes distress or impaired functioning
  - Earlier belief
    - Disorders of the body
    - Disorders of the mind
- **Human behavior**
  - Product of brain activity
- **Brain**
  - Product of two mutually interacting factors
    - Genetics (DNA determines individualism)
    - Experiences



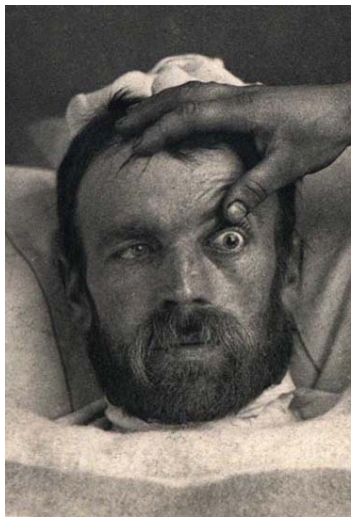
Mental Illness and the Brain

- **Psychosocial Approaches to Mental Illness**
  - Freud's theory
    - Mental illness- Unconscious and conscious elements of psyche come into conflict
  - Skinner
    - Many behaviors are learned responses to the environment
    - Mental illness as a "maladaptive behavior" that is learned
  - Psychotherapy
    - Attempt to modify, with verbal communication, the patient's response
    - Has biological basis but does not work for every mental disorder



Mental Illness and the Brain

- **Biological Approaches to Mental Illness**
  - Mental illnesses traced directly to biological causes
    - General paresis of the insane
      - Symptoms: Mania, cognitive deterioration
      - Cause: *T. pallidum brain* infection (causes syphilis)
  - Roots of mental disorders
    - Changes in brain anatomy, chemistry and function

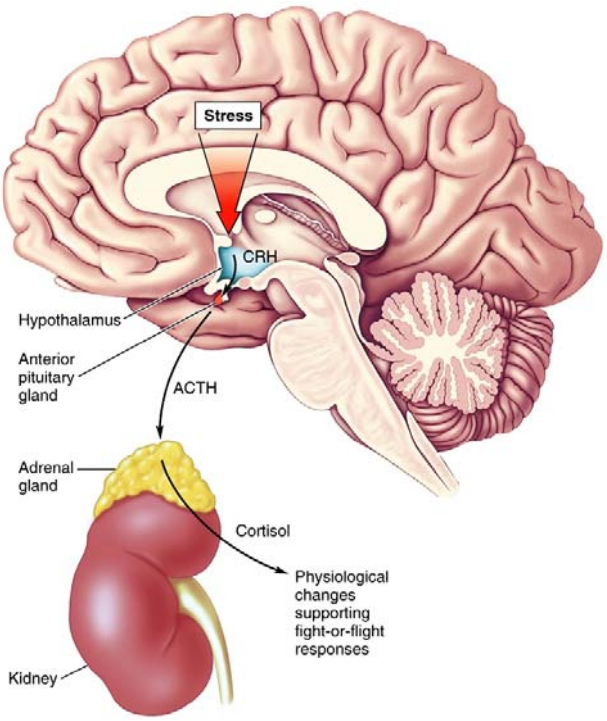


Anxiety Disorders

- **Fear**
  - An adaptive response to threatening situations
  - Innate and species-specific
  - Learned
- **Anxiety disorders**
  - Caused by inappropriate expression of fear Common Anxiety Disorders
  - Panic disorder
  - Agoraphobia
  - Obsessive-compulsive disorder
  - Generalized anxiety disorder
  - Specific phobias
  - Social phobia
  - Post-traumatic stress disorder

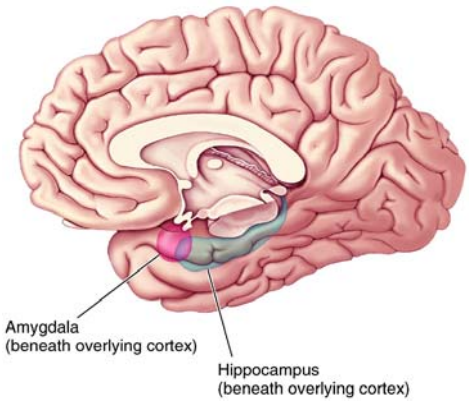
Anxiety Disorders

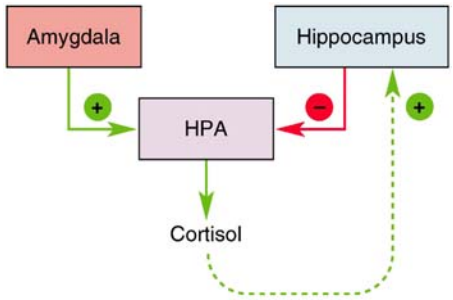
- **Biological Bases of Anxiety Disorders**
  - Fear evoked by threatening stimulus: Stressor
  - Manifested by stress response
    - Avoidance behavior
    - Increased vigilance and arousal
    - Activation of the sympathetic division of the ANS
    - Release of cortisol from the adrenal glands
  - Stimulus-response relationship strengthened (and weakened) by experience
  - Stress: Corticotropin-releasing hormone (CRH)→ adrenocorticotropic hormone (ACTH)→ cortisol



Anxiety Disorders

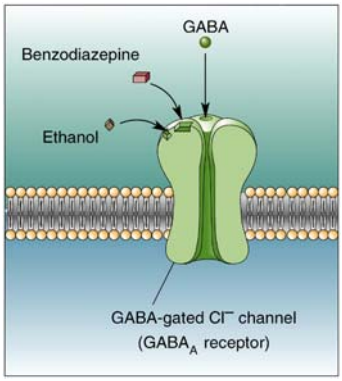
- **Biological Bases of Anxiety Disorders**
  - Regulation of the HPA Axis by the Amygdala and Hippocampus
    - Both regulate CRH neurons
    - Amygdala projects to bed nucleus of the stria terminalis, which activates the HPA axis
    - Hippocampus deactivates the HPA axis
      - Has glucocorticoid receptors
      - Serves as feedback loop
    - Push-pull style regulation

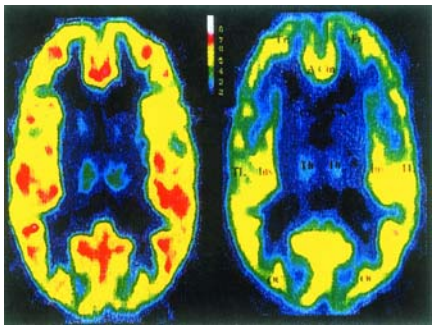




Anxiety Disorders

- **Treatments for Anxiety Disorders**
  - Psychotherapy
  - Anxiolytic Medications
    - GABA (inhibitory neurotransmitter)
      - $GABA_A$ receptor has binding sides for Benzodiazepines (e.g. valium) and ethanol
    - Serotonin-selective reuptake inhibitors (SSRIs)
      - Used to treat mood disorders but also OCD
      - Effect not immediate
      - Increase in glucocorticoid receptors in hippocampus → (-) feedback to CRH neurons in the hypothalamus
  - New drug target
    - Antagonists to CRH receptors





Diminished binding of radioactive benzodiazepine

Affective Disorders

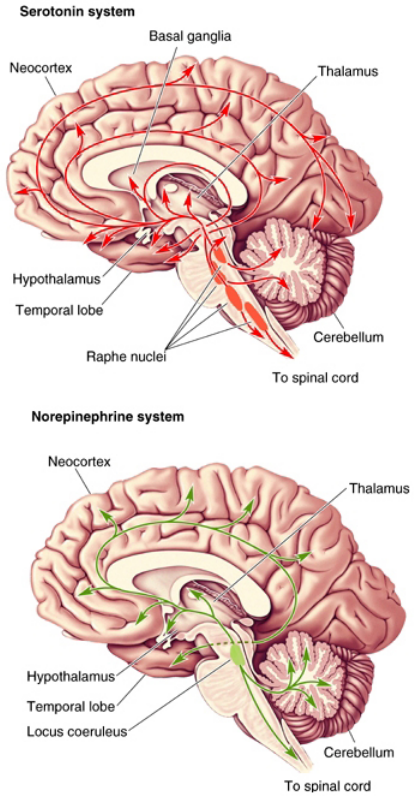
- **A Description of Affective Disorders**
  - "Mood" Disorders
    - Major Depression
    - Bipolar Disorder
  - Major Depression
    - Loss of appetite (or increased appetite)
    - Insomnia (or hypersomnia)
    - Fatigue
    - Feelings of worthlessness and guilt
    - Diminished ability to concentrate
    - Recurrent thoughts of death
  - Dysthymia
    - Milder than major depression but chronic

Affective Disorders

- **A Description of Affective Disorders**
  - Bipolar Disorder
    - Repeated episodes of mania or mixed with depression
      - Manic-depressive disorder
      - Type I (manic episodes)
      - Type II (no impairment in judgment – hypomania - but associated with depression)
    - Mania
      - Inflated self-esteem or grandiosity
      - Decreased need for sleep
      - Increased talkativeness or feelings of pressure to keep talking
      - Flight of ideas or a subjective experience that thoughts are racing
      - Distractibility
      - Increased goal-directed activity
      - Impaired judgement
    - Hypomania
    - Cyclothymia (not major depression)

Affective Disorders

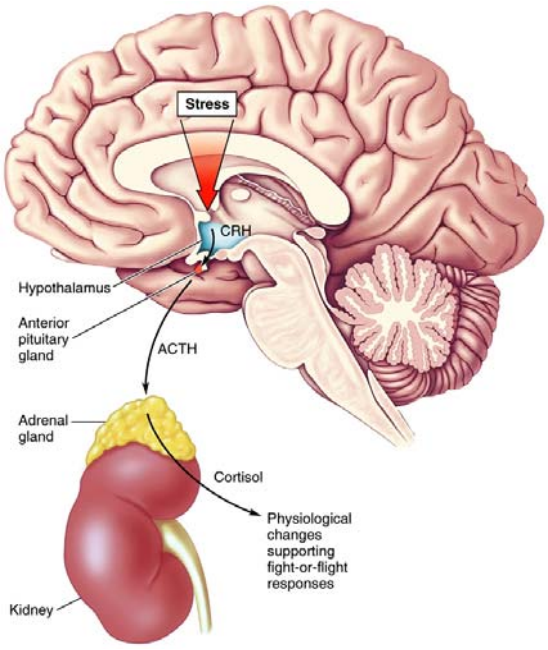
- **Biological Bases of Affective Disorders**
  - The Monoamine Hypothesis
    - Problems with diffuse modulatory systems of serotonin (5HT) and/or norepinephrine (NE)
    - Monoamine Oxidase (MAO) inhibitors
      - Increase 5HT and NE action
    - Not a simple relation
      - Direct effect of drugs on synapse but weeks for antidepressant effects
      - Cocaine (increases NE in synaptic cleft) not an antidepressant
      - Alterations in gene expression?



Biomedical Imaging and Applied Optics Laboratory

Affective Disorders

- **Biological Bases of Affective Disorders**
  - The Diathesis-Stress Hypothesis
    - Genetic and nongenetic (environmental influences) → HPA axis
    - Impact of CRH
      - Anxiety and depression often coexist
      - Hyperactive HPA system deleterious to the brain?
    - Glucocorticoid receptor
      - Expression regulated by early (but not adult) sensory experience
      - Tactile stimulation process
    - Factors of mood and anxiety disorders
      - Genes
      - Early childhood experience

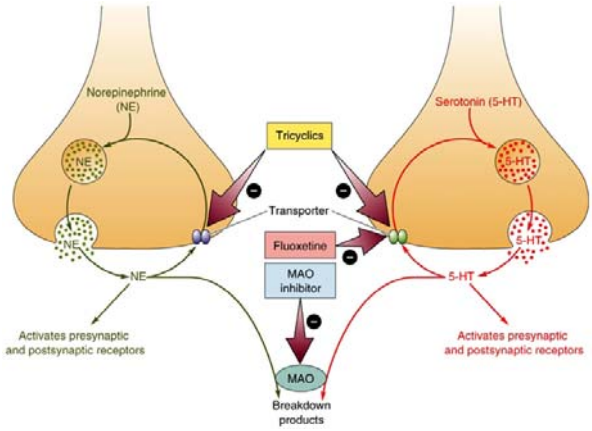


Affective Disorders

- **Treatments for Affective Disorders**
  - Electroconvulsive Therapy (ECT)
    - Localized electrical stimulation
    - Advantage of ECT: Quick relief
    - Adverse effect of ECT: Prior memories, storage of new information
    - Structures involved: Temporal lobe
  - Psychotherapy
    - Mild to moderate depression
    - Help patients overcome negative views

Affective Disorders

- **Treatments for Affective Disorders**
  - Antidepressants
    - ↓ HPA activity, ↑ glucocorticoid receptor expression in hippocampus
    - Tricyclics
      - Block reuptake of both 5HT and NE
    - 5HT-selective reuptake inhibitors (SSRI)
      - Prolonged treatment → neurogenesis in hippocampus
    - NE-selective reuptake inhibitors
    - MAO inhibitors
      - Reduce enzymatic degradation
    - CRH antagonists under development
  - Lithium
    - Interferes with second messengers inside the neurons
    - Mood-stabilizer for treatment of bipolar disorder
    - Mechanism unknown

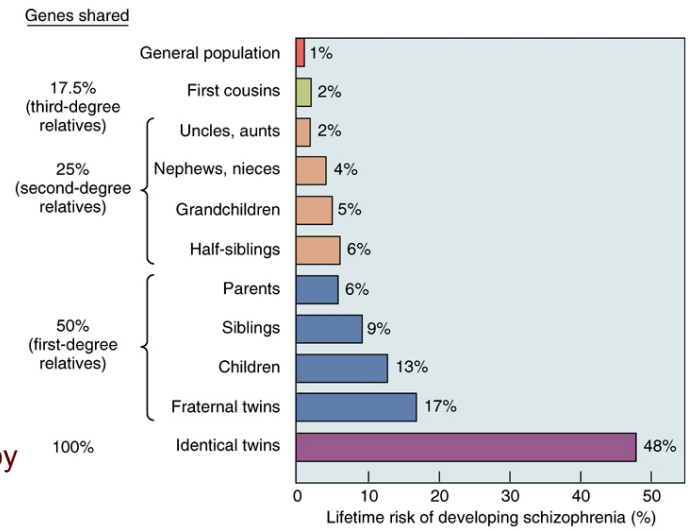


Schizophrenia

- **A Description of Schizophrenia**
  - Severe mental disorder
    - Adolescence or early adulthood
    - Loss of contact with reality
    - Disruption of thought, perception, mood and movement
  - Symptoms of schizophrenia
    - Positive
      - Delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior
    - Negative
      - Reduced expression of emotion, poverty of speech, difficulty in initiating goal-directed behavior, memory impairement
  - Three types of schizophrenia
    - Paranoid schizophrenia
    - Disorganized schizophrenia (including flat affect)
    - Catatonic schizophrenia

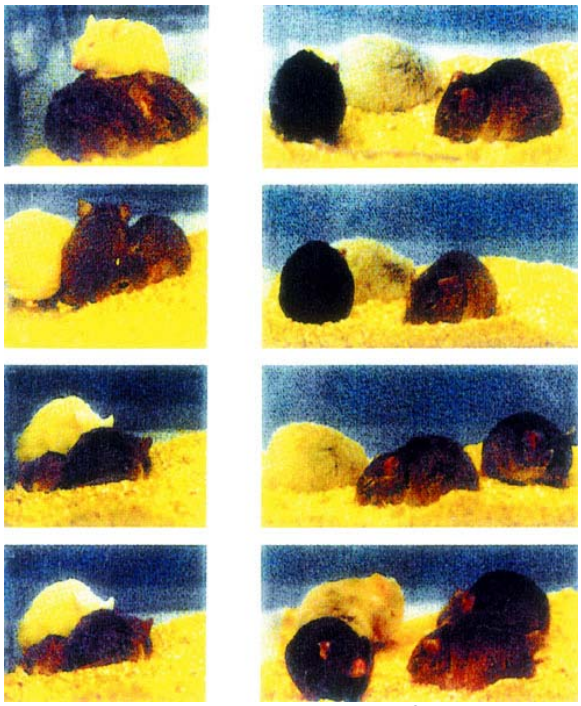
Schizophrenia

- **Biological Bases of Schizophrenia**
  - Genes and the Environment
    - Schizophrenia: A genetic disorder
    - Anatomic and microscopic differences
      - Ventricle to-brain-size ratio
      - Myelin sheaths
      - Changes in synapses and neurotransmitters (especially dopamine and glutamate)
  - The Dopamine Hypothesis
    - Psychotic episodes triggered by activation of dopamine receptors
    - Neuroleptic drugs
      - D_2 dopamine receptor blockers



Schizophrenia

- **Biological Bases of Schizophrenia**
  - The Glutamate Hypothesis
    - Glutamate
      - Fast excitatory neurotransmitter in the brain
      - Two important receptor subtypes, AMPA and NMDA
    - Behavioral effects of phencyclidine (PCP)
      - Hallucinations and paranoia
      - Inhibits NMDA receptors



Mice with normal and reduced numbers of NMDA receptors

Schizophrenia

- **Treatments for Schizophrenia**
  - Consists of drug therapy combined with psychosocial support
  - Conventional neuroleptics, such as chlorpromazine and haloperidol, act at D2 receptors
    - Reduce the positive symptoms of schizophrenia
    - Also have numerous side effects
      - Parkinsonian symptoms and tartive dyskinesia
  - Research into NMDA receptor agonist

Conclusion

- **Impact of neuroscience on psychiatry**
- **Genes and environment play an important role**