Chapter 1

Review of Basic Sciences

Relevant to Psychiatry

- **Neuroanatomy**
- **Neurophysiology**
- **Neurotransmitters**
- **Clinical Psychology**

A 70 year-old diabetic woman admitted to the medical ward because of a transient ischemic attack and dysarthria. She has disorientation, poor attention and memory impairment for several months.

The human brain contains approximately 10^{11} nerve cells (neurons) involved in information processing. The nervous system responds to changes in the external and internal environment. The anatomical organization and neurophysiology of the human brain are of particular relevance for psychiatric disorders. Because of their clinical relevance and importance, medical students in psychiatry clerkship should review basic neurosciences.

REVIEW OF NEUROANATOMY & NEUROPHYSIOLOGY

❑ Frontal Lobe Functions

- Cognitive and intellectual functions:
  Attention, concentration, registration, orientation (to time,place,and person) reasoning, understanding, analysis, comparison, critical thinking , problem- solving, planning and judgment.
- Control of behavior/ voluntary movements/ sphincters.
- Motor language: processing information to produce speech(dominant frontal).
- Control of emotion: right frontal lope contains negative emotions (anger/fear…), whereas left frontal lope controls such negative emotions and contains positive emotions. Brain lesions affecting left frontal lope lead to exaggeration of fear and worries, whereas lesions affecting right hemisphere lead to unusual euphoria and inappropriate laughter.

❑ Temporal Lobe Functions

- Retention and comprehension of auditory and visual information.
- Recall of recently registered information (dominant hippocampus).
- Emotions and sexual activity.

- **Parietal Lobe Functions**
  - Interpretation of sensations: touch, pressure (stereognosis).
  - Appreciation of body image (spatial orientation).
  - Constructional skills: dressing, drawing … (non-dominant lobe).

- **Occipital Lobe Functions**
  - Perception and analysis of visual sensations (color, shape, dimensions…).

- **Cerebellum Functions**
  - Coordination of muscle contractions and motor activity.
  - Maintenance of posture and body balance.

- **Basal Ganglia Functions**
  - Subconscious control of tone and movements of the skeletal muscles, such as swinging the arms while walking.

- **Midbrain Functions**
  - Consciousness and arousal (function of the reticular formation which extends also through pons and medulla).
  - Control of reflexive head and eye movements.
  - Raphe nuclei function: serotonergic neurons in the brainstem projecting to a large number of brain structures.

- **Pons Functions**
  - Connection of various parts of the brain with each other.
  - Cranial nerve functions (5, 6, 7 and 8).
  - ***Locus Cerulus*** is the most important noradrenergic nucleus in the brain, which has very high density of noradrenaline neurons, and numerous projections to other brain regions; especially the cortex and hippocampus. It is essential for the behavioral and physiological expression of anxiety and fear.

- **Medulla Functions**
  - Medulla contains vital and non-vital centers.
    - –Vital centers: cardiac, respiratory and vasomotor centers.
    - –Non-vital centers: vomiting, swallowing, sneezing, coughing and hiccupping centers.
  - Cranial nerves functions (9,10 & 11).
  - Connection of the spinal cord with the brain.

- **Functions of Reticular Formation System:**
  - Consciousness and alertness.
  - Control of skeletal muscles.
  - Control of somatic and visceral sensations.

- **Functions of the Thalamus:**
  - Sensory relay station: processing tactile, proprioceptive, pain and temperature information, sending it to sensory cortical areas.
  - Integrating a large variety of sensory and motor information, and the relation of this information to one's emotional feelings, subjective states and personality.
  - Influencing the level of consciousness and alertness through connections with the reticular formation and cortical centers.

- **Functions of the Hypothalamus**

  Hypothalamus preserves body homeostasis through:
  - **Regulation of food intake**:

    Feeding / hunger center, located in the lateral side of hypothalamus, which is chronically active and its activity is transiently inhibited by activity in the satiety center, located in the ventro-medial side, after the ingestion of food.
  - **Regulation of water intake** (superiolateral part of Hypothalamus).
  - **Regulations of 24-hour sleep-wake cycle** (suprachiasmatic nucleus: light reduces melatonin in pineal gland whereas darkness enhances melatonin secretion).

- **Regulation of temperature:**
  - Antirising center in the anterior hypothalamus, mediates the parasympathetic system to increase body heat loss, thus reducing body temperature.
  - Antidrop center in the posterior hypothalamus mediates the sympathetic system to reduce body heat loss.
- **Higher control of hormones:**
  Catecholamines-vasopressin-oxytocin-ACTH-TSH-FSH-LH-Prolactin and growth hormones .
- **Higher control of the autonomic nervous system**
  - Parasympathetic (by anterior hypothalamus)
  - Sympathetic (by posterior hypothalamus)

❑ The Autonomic Nervous System

It is distributed throughout the central and peripheral nervous system, divided into two parts: the sympathetic and the parasympathetic.

- **The sympathetic nervous system::**
  Beta 1 stimulation : accelerates the heart rate and increases myocardial contractility.
  Beta 2 stimulation: vasodilatation of coronary artries,bronchodilatation relaxation of uterus, intestines and bladder, and skeletal muscle vasodilatation.
  Alpha receptor stimulation : constriction of the arterioles of the skin and intestine .It dilates iris (mydriasis), closes the sphincters, decreases secretion of salivary glands , piloerection, sweating and ejaculation .
- **The parasympathetic nervous system**
  It aims at conserving and restoring energy. It slows the heart rate; constricts the pupils; increases peristalsis of the intestine and glandular activities (increasing secretions); opens the sphincters and contracts the bladder wall. The parasympathetic neurons also facilitate erection.

- **Limbic System**
  - **Components:**
    Cingulate gyrus - Hippocampus(temporal lobe) - Amygdala - Parahippocampal gyrus - Hypothalamus - Anterior nucleus of thalamus - Major tracts connecting the system
  - **Functions:**
    - Emotional and behavioral responses (fear, rage …).
    - Sexual feelings and pleasure: norepinephrine is involved in ejaculation (males) and orgasm (females).
    - Recent memory.
    - Neocortical activities modify emotional behavior and vice versa. However, one of the characteristics of emotion is that it cannot be turned on and off at will. Another characteristic of limbic circuits is their prolonged after-discharge following stimulation. This may explain in part the fact that emotional responses are generally prolonged rather than evanescent and outlast the stimuli that initiate them.

- **The Gate Control Theory of Pain**
  Cortical and subcortical centers process and filter afferent pain impulse through a gating mechanism in the dorsal horn of the spinal cord. Competing signals and neurotransmitters can open or close the gate on painful perceptions. Serotonin in descending pathways has an inhibitory effect, i.e., closing the gate. Endorphin deficiency seems to correlate with the augmentation of afferent stimuli. Substance P is involved in altering the pain threshold. Thus, neurobiological factors play a large role in the onset and perpetuation of pain experience.

REVIEW OF NEUROTRANSMITTERS

1 . SEROTONIN (5 Hydroxytryptamine = 5HT)

Serotonin is an indolamine synthesized from an essential amino acid L-tryptophan, found in the gastrointestinal tract, platelets, monocytes (5HT1A:enhance activity of natural killer cells

/psychoneuroimmunity), the brain and the spinal cord. The major site of serotonergic cell bodies in the brain is the raphe nuclei in the brainstem, from which fibers project to many brain structures, these include projections to:

- Frontal cortex: regulation of emotional reaction to stress and impulsive behavior (5HT1A).
- Limbic system: anxiety and panic feelings (5HT 2A-2C).
- Basal ganglia: movement control and compulsions (5HT2A).
- Hypothalamus: appetite and eating regulation (5HT3).
- Brainstem chemoreceptor trigger zone: vomiting (5HT3).
- Brainstem sleep centers: deep sleep (5HT2A).
- The ingestion of foods rich in tryptophan rapidly increases brain serotonin synthesis, which accounts for their mild sedating effects.
- Spinal cord: sexual spinal responses, orgasm (5HT2A).
- Peripheral serotonergic receptors (5HT3,4&7) in the intestine regulate intestinal secretions and motility.

Serotonin deficiency is found in depression, anxiety, panic disorder, phobias, obsessive compulsive disorder and bulimia nervosa.

Serotonin is metabolized to an inactive metabolite by MAO-A enzyme.

2. DOPAMINE

Dopamine is a catecholamine synthesized from tyrosine. There are 4 most important dopaminergic tracts:

1. *The mesolimbic dopamine pathway*: emotional behavior, reward reinforcement , pleasure feelings and sex drive. Pathological hyperactivity of this pathway accounts for active (positive) psychosis (hallucinations, delusions, aggression…)

Nucleus accumbens is a dopamenergic nucleus , located in the mesolimbic pathway, involved in the physiological reward system. Its reinforcing effects are stimulated by caffeine, nicotine, cocaine

and other CNS stimulants. Its stimulation increases sex desire and behavioral response, and suppresses appetite.

2. *The mesocortical dopamine pathway*: mental arousal and cognitive functions. Pathological underactivity of this pathway (mesocortical defect: due to glutamate excitotoxic overactivity,primary dopamine neuron defect or serotonergic overactivity) is responsible for most negative features and cognitive defects seen in some schizophrenic patients.
3. *The nigrostriatal tract*: low dopamine levels are associated with motor symptoms of Parkinson's disease. Antidopaminergic drugs lead to Parkinsonian extrapyramide side effects. Serotonin 2A receptors on dopamine neurons inhibit dopamine release.
4. *The tuberoinfundibular tract*: dopamine inhibits prolactin release from the anterior pituitary.

Dopamine Receptors:

- D_1 receptors may play a role in negative symptoms (D_1 antagonist treat negative symptoms).
- D_2 receptors blocked by anti-psychotic drugs for the treatment of positive psychotic symptoms. D_2 agonists are used for the treatment of Parkinson's disease.
- Other dopamenergic receptors (D_3, D_4 & D_5) : it is not clear to what extent these receptors contribute to the clinical properties of anti-psychotic drugs.

  Serotonin-Dopamine Interactions:

  Serotonin inhibits dopamine release in various dopamine pathways(understanding this is critical to understanding atypical antipsychotics).

3. NORADRENALINE (NOREPINEPHRINE)

Noradrenaline is a catecholamine synthesized through hydroxylation of dopamine. The major concentration of noradrenergic cell bodies in the brain is in the locus Cerulus from which neurons project to:

- *Frontal cortex*: regulation of mood (Beta 1 receptors) and regulation of cognitive functions (Alpha-2 receptors)

- *Limbic system*: energy, emotions and psychomotor activity control.
- *Cerebellum*: regulation of motor movements.
- *Cardiovascular centers in the brainstem*: -blood pressure regulation.

Noradrenergic innervation regulates the heart rate (via Beta 1 receptors in sympathetic neurons) and controls bladder emptying (via Alpha –receptors). Alpha –2 presynaptic noradrenergic autoreceptors (on adrenergic neurons) and heteroreceptors (on seretonergic neurons) have a negative feedback effect; inhibiting excessive release of noradrenaline and serotonin respectively.
Noradrenaline at low concentrations has stimulatory effects on immune function but it inhibits effects at high concentrations.
Noradrenaline is involved in ejaculation in men and orgasm in women.

Noradrenaline – Serotonin Interactions

There are two types of presynaptic noradrenergic receptors on serotonin neurons that regulate serotonin release:

- Alpha – 2 heteroreceptors (in the cortex): when stimulated they turn off serotonin release.
- Alpha –1 receptors (in the brainstem; a pathway from locus Cerulus to raphe nuclei), when stimulated these receptors enhance serotonin release.

4. ACETYLCHOLINE (ACH)

Acetylcholine is synthesized from choline and acetyl coenzyme A. The major brain center for cholinergic neurons is *the nucleus basalis of Meynert,* which projects to cerebral cortex and the limbic system. These neurons have the principal role in mediating short-term memory. Additional cholinergic neurons are found in:

- The reticular formation: REM –sleep induction.
- Basal ganglia(extrapyramidal tract) and cerebellum : regulation of body posture, muscle tone and motor movements.

- The autonomic nervous system; parasympathetic (both pre and post synaptic pathways) some sympathetic pathways (presynaptic/sweet glands).
- Acetylcholine is involved in erection. N.B.: nitric oxide (NO), not nitrous oxide (N2O), is also involved in erection .It is synthesized in the body from l-arginine.

5. GAMA AMINOBUTYRIC ACID (GABA)

GABA is an amino acid neurotransmitter with a very fast inhibitory action. It is found almost exclusively in the brain, and synthesized from glutamate.

GABA is thought to suppress seizure activity, anxiety and mania. There are three types of GABA receptors A,B&C. The GABA-A receptors have binding sites for benzodiazepines and barbiturates, which increase the affinity of the GABA-A receptors for GABA.

6. GLUTAMATE

Glutamate is an amino acid excitatory neurotransmitter. It is synthesized from deamination of glutamine. Many sensory organs – including the cochlea, the olfactory bulb, the retina and thalamocortical fibers – use glutamate as their principal neurotransmitter. Pyramidal neurons in the cortex are glutamartergic. Glutamate is involved in the highly organized information flow through the brain. In the hippocampus, glutamate may be specifically relevant to the pathophysiology of dementing illness(Alzheimer's disease). Glutamate excitotoxicity is suggested as a possible cause of neuronal degeneration in schizophrenic patients with negative features.

Sigma receptors(1&2) : these were thought of as opioid receptors but later on found to be related to glutamate receptors (NMDA) and involved in enhancement of memory and cognitive functions , when stimulated by fluvoxamine they improved the negative symptoms in schizophrenic patients.

7. SUBSTANCE – P

It is an excitatory neurotransmitter associated with mediation of pain perception and thought to play an important role in the

pathogenesis of migraine, cluster headache and chronic pain. Abnormalities affecting substance P have also been hypothesized for mood disorders, Alzheimer's dementia and Huntington's disease.

8. HISTAMINE

Histamine is synthesized from histidine. In the brain it is located in the hypothalamus and fibers projecting to cerebral cortex, the limbic system, and the thalamus. There are three types of histamine receptors: H1 receptors regulate appetite and arousal and have a role in allergic symptoms. When antihistamines are used for allergic symptoms they exert marked sedative effects and weight gain; H2 receptors are involved in gastric acid output; when H2 – receptors antagonist are used they heal gastric and duodenal ulcers, H3 receptors; stimulation of these receptors thought to be expressed on histamine nerve terminals, suppresses histamine release.

9. MELATONIN

Hypnotic hormone produced by the pineal gland stimulated by darkness and inhibited by light (suprachiasmatic nucleus),involved in regulation of sleep-wake 24-hour cycle.

10. ENDOGENOUS OPIOIDS

Enkephalins, endorphins and dynorphins are involved through their receptors (mu,kappa and delta) in many mental functions : pain perception (analgesics), learning, memory, mood and dependence.

CLINICAL PSYCHOLOGY

1. LEARNING THEORIES

There are three basic learning theories:

I. Classical Conditioning II. Operant Conditioning III. Modeling

- Learning: a relatively permanent change in behavior brought about by prior experience.

I. Classical Conditioning

Stage 1: Unconditioned stimulus (e.g. food) > Unconditioned response (e.g. salivation)

Stage 2: Conditioned stimulus (e.g. sound of the bell) + Unconditioned stimulus (food) > Unconditioned response (salivation).

Stage 3: Condition stimulus (sound of the bell) > Conditioned response (salivation)

II. Operant Conditioning

Behavior, which is followed by advantageous consequences, is likely to be repeated, whereas behavior followed by noxious consequences will become less frequent.

- Reinforcement: the process of increasing the frequency of a particular piece of behavior by presenting a reinforcing stimulus.

Positive reinforcement : enhancement of behavior by a desired reward.

Negative reinforcement : enhancement of behavior by removal / avoidance of undesirable event.

III. Modeling occurs when the behavior of an individual(the observer) is affected by the opportunity to observe the behavior of another person (the model).

Clinical Uses of Learning Theories: (see Chapter 24)

- Treatment of phobias (systemic desensitization flooding).
- Treatment of obsessive rituals (modeling, response prevention).
- Relaxation training (for anxiety).
- Aversion therapy (for alcoholism and sexual deviation).

2. COGNITIVE THEORY

It emphasizes the impact of interpretation of events, expectations, and process of thinking about oneself, people, the environment, the past, and the future on the mood and behavior. Depression and anxiety result from, and complicated by, wrong automatic thoughts e.g. "I am bad person". Correction of erroneous thoughts with cognitive therapy usually relieves patients from negative emotions (see cognitive therapy Chapter 24 for clinical applications in psychiatry).

3. PSYCHOANALYSIS

A -Topographic model of the mind

This model divides the mind into three regions:

1. The conscious 2. The unconscious 3. The preconscious

Each of which has its own characteristics:

1. **The conscious:** The part of the mind in which perceptions coming from the mind, the body and from the outside world are brought into awareness. It's content can be communicated by means of language or behavior.
2. **The unconscious:** The part of the mind that contains the instinctual wishes and drives (self-preservative drives and sexual instincts) and represses them; keeping them out pf conscious awareness through resistance to remembering.
3. **The preconscious:** The part of the mind that comprises those mental processes, contents and events that are capable of being brought into conscious awareness by deliberate focusing of attention on the memory.

B - Structural Theory Model (Ego Psychology)

This model divides the psychic apparatus into the id, the ego and the super ego.

1. **The " id ":** It includes the unconscious instinctual whishes and drives, and operates according to the pleasure principle (it lacks the capacity to delay or modify the instinctual drives).
2. **The " ego ":** It attempts to achieve and coordinate optimal gratification of instinctual wishes and drives while maintaining good relations with the demands of the outer world and external reality.
3. **The " superego":** It includes internalized moral values, prohibitions and standards; and offers approval or disapproval. The superego conducts an ongoing scrutiny of the person's feelings, thoughts, and behavior. It establishes and maintains the persons moral conscience.

- **Defense Mechanism:**

These are dynamic psychological strategies used by a person to deal with unpleasant situations or distressing internal conflicts, to manage instincts drives or affect (see Chapter 5).

4. INTELLIGENCE TESTING

Intelligence is the ability to solve environmental problems and to adapt to changes.

- Intelligence tests include:

A. Binet test:

$$\text{Intelligence Quotient (IQ)} = \frac{\text{Mental age X 100}}{\text{Chronological age}}$$

B. Wechsler tests (for children and adults).

The tests include two sections verbal and performance.

IQ scores:

Average Normal	= 100 ± 10
Bright Normal	= 120
Superior	≥ 130
Dull Normal	= 80 -90
Borderline	= 70 -79
Mild Mental Retardation	= 50 - 70
Moderate Mental Retardation	= 35 - 49
Severe Mental Retardation	= 20 - 34
Profound Mental Retardation	= below 20

5. PERSONALITY TESTING:

Personality is the distinctive and characteristic patterns of thought, emotion, and behavior that define an individual's personal style and influence his or her interactions with the environment. The objective assessment of personality serves a number of practical needs in clinical psychiatry. Good personality test must have reliability and validity.

Reliability: the extent to which there is repeatability of consistent results.

Validity: the extent to which a test measures what it is designed to measure.

There are many personality tests. The two main tests widely used in clinical practice are:

- Eysenck Personality Inventory (EPI) : It measures the following personality dimensions: extroversion (vs. introversion), neuroticism (vs. stability), psychoticism (vs. stability).

- Minnesota Multiphasic Personality Inventory (MMPI). It consists of "yes" or "no" self-answered questions. The results are given as scores in 10 subscales.

Several intelligence and personality tests are available in Arabic language, and validated in some Arabic communities.

The clinical psychologist plays an important role within the psychiatric team for both patient's assessment (Personality, IQ…) and treatment (behavior, cognitive, psychodynamic…..).