USMLE

Step 1 lecture Notes

2019 Edition

Psychiatry

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WORLD CLASS EDUCATION FOR DOCTORS

Transference and Countertransference:

Outline:

- Transference
  - Definition
  - Case Example
  - Effect on Therapy
- Countertransference
  - Definition
  - Case Example
  - Effect on Therapy
- References

Transference:

Definition:

The patient projects feelings and personal experiences about an important person onto the therapist. Such feelings can be positive or negative. The nature of the feelings that the patient might have are dependent on stereotypical, and situational behaviors or attributes of the therapist.

The patient will transfer a response based on internal construction of the therapist, and this response will affect the alliance with the therapist.

Case example:

The patient suffers from depression. Psycho-analysis approach reveal that the possible trauma of being raised by a neglecting mother to be the main struggle for the patient. The mother always said that she does not have time for her daughter, she was always late, and that she thinks her daughter is boring. The mother always humiliated her.

The therapist has the following stereotypical attributes: she is a well-dressed woman who is very attentive and always on time. She listens carefully to the patient in every session.

The therapist at the end of today's session state that she needs to finish this session earlier because she is needed for an emergency consultation at the hospital. The patient agrees, but in her mind she starts to think that the therapist must think that I am boring and that is why she wanted me to leave earlier. Now, the patient thinks of the therapist as a mother-figure and started to transfer negative feelings onto her. The patient calls before her next scheduled session and states that she would like to cancel her next appointment. When the therapist asks her why, she states that she is sure the therapist has better use of her time than spending it on her.

Analysis of the above scenario:

- Things were going well for this patient, until she transferred her feelings about her mother onto the therapist
- The therapist did not do anything wrong, as she had an emergency appointment
- The therapist tried to ask the patient why she wants to cancel in an attempt because she thought transference might have occurred

- She wanted the patient to understand that she cares if she comes or not and she is interested in treating her

Effect on therapy:

- If the therapist does not recognize the possibility of transference, the patient will start to transfer positive or negative feelings onto the therapist
- The patient might choose to go with the therapist treatment plan because of these feelings
- On the other hand, if the patient develops negative feelings, this can result in less adherence to the therapy

Countertransference:

Definition:

The moment that you recognize the patient might start to project feelings about an important person onto the therapist, you will come to realize that the opposite can also happen. In this case, the doctor might project feelings about an important person in his or her life onto the patient.

Case example:

A therapist has been working with a patient for one year. The patient suffers from gambling disorder and he keeps talking about his daughter and how she keeps controlling his spending and that he does not like that.

The therapist father had a gambling problem that left her family broke. Because of this, the father eventually left her and her mother when she was young.

Back to the session, the patient states that his daughter should not have the authority to tell him what to do with his money. And he states that he is the one who is paying for her college. At some point, the patient states that he is going to stop paying for her college.

The therapist thinks for a moment that the patient is abandoning his daughter just like her father abandoned her. She sees that the therapy sessions are not helping the patient as she would have hoped. She no longer looks forward to seeing the patient and she wishes if the patient would cancel the next session.

Because she stopped paying attention for a moment, the patient notices. He states that this therapy thing is expensive and is not working and he states he does not see the point of having these sessions.

Analysis of the above scenario:

- The therapist thinks that this is because of countertransference
- She transferred her feelings about her own father onto her patient
- Because of this, she is no longer interested in the patient

Effects on therapy:

- If the therapist transfers her feelings onto the patient, this will influence the patient-doctor relationship
- If the transferred feelings are positive, this can result in inappropriate relationship with the patient or in forming feelings of guilt if the patient commits suicide for example

- On the other hand, if the feelings that are transferred are negative, this can result in less than optimal performance from the therapist

References:

- First-Aid 2018

Defense Mechanisms:

Outline:

- Definition
- Individual Psyche Structures
- Classification
- Pathological Defense Mechanisms
- Immature Defense Mechanisms
- Neurotic Defense Mechanisms
- Mature Defense Mechanisms
- References

Definition:

Defense mechanisms are unconscious psychological mechanisms that our ego uses to protect our psychological integrity in a given situation or stimulus. These defense mechanisms can result in healthy or unhealthy (mental illness) consequences.

Individual Psyche Structures:

Id:

This is the unconscious drive forces a person to seek what he or she wants. These needs are selfish and childish. This part of the psyche has no ability to delay instant gratification.

Example:

Someone wants to have sex.

Superego:

This is a group of morals that the individual has gained from societal and parental standards of what is considered as good and bad.

Example:

That person who wants to have sex knows going to a prostitute is wrong.

Ego:

This is a moderator between pleasure sought by the id and the morals of the superego.

Example:

That person who wanted to have sex gets into a long-term relationship and now has a girlfriend. Their relationship is healthy and is way more than just having sex like the id wanted at first.

Classification:

Defense mechanisms can be seen in a hierarchy perspective. Depending on the developmental maturity of the individual and the individual's ability to cope with a new trauma, four different levels of defense mechanisms can be employed.

- Level I defense mechanisms are pathological or psychotic. They are the least immature and can often lead to mental illness
- Level II defense mechanisms are immature. They are unhealthy and can lead to mental illness. However, they are not pathological
- Level III defense mechanisms are intermediate or neurotic. These are somewhere in between normal and immature defense mechanisms
- Level IV defense mechanisms are mature or normal. Under trauma, the individual is still expected to show some sort of a defense mechanism to the psyche or ego. When this defense mechanism is appropriate and constructive, it will be considered as mature

Pathological Defense Mechanisms:

- These are very pathological defense mechanisms
- People who show them are viewed as irrational or insane by others
- They aim in rearranging external experiences in an attempt to avoid coping with reality
- While they are found in psychosis, these defense mechanisms can be normal in children or when we dream

Denial:

Refusal to accept external reality. The patient tries to not argue about an anxiety-provoking stimulus by stating that it does not exist. This type of defense mechanism might be seen in some patients with physical disease such as cancer in the early stages after they receive the news.

Distortion:

Instead of denying the traumatic reality, the patient might reshape the external reality to meet what he or she wants

Immature Defense Mechanisms:

- These defense mechanisms are seen in adults
- These defense mechanisms, if extensively used, can be seen as socially undesirable
- Overuse of these mechanisms can lead to unhealthy consequences such as inability to cope with future stressors
- These defense mechanisms are common in patients with major depression disorder and personality disorders

Schizoid fantasy:

The patient retreats into fantasy in an attempt to avoid dealing with inner or outer conflicts and stressors.

Acting out:

Expressing unacceptable feelings or thoughts through actions without consciously choosing to.

Passive-aggressive behavior:

Hostile feelings and indirect opposition even when in a nonconfrontational situation.

Example:

An employee who is not satisfied with his work conditions might always come late to work, however he might not admit he is doing this in an attempt to get back at the employer.

Projection:

Attributing an unacceptable internal thought or impulse to an external source.

Example:

An employee who thinks he is making too little at his job in a restaurant thinks about taking some money. He then claims that the employer is doing a scam to not pay work insurance for the employee.

Neurotic Defense Mechanisms:

- These are common defense mechanisms in adults
- They have short-term benefits in coping
- Unfortunately, the long-term effect is usually negative on social and occupational life of the patient

Displacement:

Redirection of emotions or impulses to a third neutral party.

Example:

The same employee from above who had an impulse about stealing from his employer might tell his wife that she is spending too much on shopping and that is why they have a financial issue.

Dissociation:

Transient, but drastic, change in personality, memory or motor behavior to avoid emotional stress. The patient will not remember the traumatic event, or have an incomplete recall.

Example:

A young woman is walking in the street in her old town. She sees someone and then becomes numb and detached. That person has sexually abused her when she was in high-school. Later on, her friends tell her what is wrong and she does not know why she felt numb and detached for a moment.

Intellectualization:

Focusing on the logic and factual part of a problem in an attempt to distance someone's self from the emotional distress that the stressor might cause.

Reaction formation:

Replacement of a negative impulse or wish with a positive feeling or idea, even though it is not what the patient really wants to express.

Example:

A patient with lustful thoughts about his wife's friend takes his wife out for a fancy and romantic dinner.

Repression:

Subconsciously withholding an impulse or a feeling that is known to the patient to result in suffering or to be dangerous.

Example:

A patient who has social anxiety does not recall that his father used to verbally abuse his mother for years when he was a child.

Regression:

Regressing to an earlier developmental stage when coping with a stressor.

Example:

Someone's mother has just died. He is crying, even though, he knows how to speak and say that he is sorry. Whining can be seen as a defense mechanism here.

Isolation:

Separating emotions from ideas and events.

Example:

An eye-witness is stating a graphic murder without feeling upset or sad about what he or she is describing in the court.

Mature Defense Mechanisms:

- Emotionally healthy adults use these defense mechanisms to cope with stressors
- They optimize the individual's social and occupational life
- The goal in most psychodynamic approaches in psychotherapy is to help the patient to use these defense mechanisms instead of the immature or pathological ones

Suppression:

Consciously choosing to delay attention to an idea, or an impulse to cope with the current situation or reality.

Example:

A medical graduate chooses to suppress thinking about the results of the matching process until they become available and he knows which residency program he was accepted at.

Anticipation:

Realistic planning for a known future problem or discomfort.

Example:

Studying before an exam.

Altruism:

Alleviating negative feelings by providing constructive service to others to bring them pleasure.

Example:

A banker decides to give a substantial amount of money to help those with bank loans to help them payback their debts.

Sublimation:

Transforming unhelpful and negative instincts into healthy actions and behaviors.

Example:

An aggressive person joins the football team to transform his aggression into a game.

Humor:

Appreciating the amusing or funny nature of a stressor.

Example:

A student has an upcoming neurology exam. He jokes with his colleagues about how the body is presented in the motor cortex.

References:

- First-Aid 2018

Attention Deficit Hyperactivity Disorder:

Outline:

- Definition
- Risk factors
- Clinical findings
- Treatment
- References

Definition:

Attention deficit hyperactivity disorder is characterized by an ongoing pattern of inattention and/or hyperactive impulsivity in a child that interferes with functioning and development.

Risk Factors:

- Family history
- Exposure to cigarettes, alcohol, or illicit drug use during pregnancy
- Exposure to high levels of lead at a young age
- History of traumatic brain injury
- Low birth weight
- More common in males

Clinical Findings:

Normal intelligence but can be associated with learning difficulties. DSM-5 criteria are used to diagnose attention deficit hyperactivity disorder.

Diagnostic criteria:

A. A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development characterized by 1. and/or 2.
    1. Inattention: Six or more of the following, persisted for six months or more:
        i. Fails to pay attention to details
        ii. Difficulty sustaining attention in tasks
        iii. Does not seem to listen when spoken to
        iv. Does not follow through on instructions
        v. Problems with organizing tasks, or keeping things in order
        vi. Does not engage in tasks that require focusing or attention
        vii. Often loses necessary thinks like mobile phones or keys
        viii. Forgetful to daily activities
    2. Hyperactivity and impulsivity: six or more of the following, for six months or more:
        i. Often Fidgets or squirms in seat often
        ii. Often leaves seat in situations where seating is expected
        iii. Often runs in situations where it is inappropriate
        iv. Often unable to engage in leisure activities quietly
        v. Often on the go as described by the parents
        vi. Often talks too much
        vii. Often answers a question before the question is completed

viii. Often has problems in waiting for his or her turn
ix. Often interrupts others

B. Symptoms were present before 12 years
C. Symptoms are present in two or more different situations or places (school, home, with friends and parents)
D. Symptoms reduce quality of life
E. Symptoms cannot be explained by another psychiatric or medical disorder

Treatment:

Cognitive behavioral therapy

Drugs:

- CNS stimulant: methylphenidate
- Atomoxetine
- Guanfacine
- Clonidine

References:

- First-Aid 2018

Oppositional Defiant Disorder and Conduct Disorder:

Outline:

- Definition of ODD
- Clinical Findings of ODD
- Treatment of ODD
- Definition of Conduct Disorder
- Clinical Findings of Conduct Disorder
- Treatment of Conduct Disorder
- References

Definition of ODD:

A pattern of hostile defiant behavior against authority figures in the absence of serious violations of social norms. This is a childhood/early-onset disorder.

Clinical Findings of ODD:

DSM-5 criteria are used to diagnose oppositional defiant disorder.

Diagnostic criteria:

A. Angry or irritable mood, defiant behavior, or vindictiveness for at least six months by showing at least four of the following symptoms and the second individual cannot be a sibling:
    1. Often loses temper
    2. Easily annoyed
    3. Often angry
    4. Often argues with authority figure “for children this is usually an adult”
    5. Often defies to comply with the authority figure requests
    6. Often annoys others
    7. Often blames others for his/her mistakes
    8. Has been vindictive at least twice within the past six months
B. The symptoms should be associated with significant distress in the individual’s immediate social context or impact his/her social, educational and occupational functioning
C. Symptoms cannot be explained by another psychiatric or medical disorder

Treatment of ODD:

Cognitive behavioral therapy

Definition of Conduct Disorder:

Repetitive and pervasive behavior that violates the basic rights of others or societal norms by an individual who is younger than 18 years of age. Those older than 18 are reclassified as antisocial personality disorder.

Clinical Findings of Conduct Disorder:

DSM-5 criteria are used to diagnose conduct disorder.

Diagnostic criteria:

A. Repetitive and persistent pattern of behavior where the basic rights of others and social norms are violated by the presence of at least three of the following in the last 12 months with one of them present in the last 6 months:
    1. Aggression to people and animals by bullying others, starting fights, being cruel to people or to animals
    2. Destruction of property by setting fire to cause serious damage or other means
    3. Theft and deceitfulness by breaking into someone's house or building, or obtaining favors by lying to others
    4. Violation of rules by staying at night despite parental prohibitions or has run away from home overnight at least twice while living with the parents

B. The symptoms should be associated with significant distress in the individual's immediate social context or impact his/her social, educational and occupational functioning

C. Symptoms onset before 18 years of age and cannot be explained by another medical or psychiatric disorder

Treatment:

Cognitive behavioral therapy

References:

- First-Aid 2018

Separation Anxiety Disorder:

Outline:

- Definition
- Clinical findings
- Treatment
- References

Definition:

The presence and persistence of overwhelming fear of separation from an attachment figure lasting for four weeks or more in a child that is older than four years. This behavior is considered as normal in children younger than 4 years.

Clinical Findings:

DSM-5 criteria are used to diagnose separation anxiety disorder.

Diagnostic criteria:

A. Persistence of three or more of the following symptoms for four weeks or more
    1. Recurrent distress when anticipating separation from attachment figures
    2. Excessive worry about losing attachment figures
    3. Excessive worry about being in a situation that can cause separation from attachment figures
    4. Refusal to go out away from home
    5. Refusal to sleep away from home
    6. Repeated nightmares of separation
    7. Repeated complaints of factitious physical symptoms to avoid separation
B. Symptoms cannot be explained by resistance to change as seen in autism spectrum disorder or any other psychiatric disorder

Treatment:

While the symptoms might seem benign, they can lead to factitious physical complaints to avoid school or being separated. Treatment options include:

- Cognitive behavioral therapy
- Play therapy
- Family therapy

References:

- First-Aid 2018

Tourette Syndrome:

Outline:

- Definition
- Epidemiology
- Etiology
- Pathophysiology
- Diagnosis
- Treatment
- References

Definition:

Tourette syndrome is a genetic neurological disorder and also a psychiatric disorder that is characterized by chronic motor and vocal tics beginning before adulthood.

Epidemiology:

- The estimated prevalence is 0.7%
- More common in children from white ethnic background
- More common in boys
- The condition persists throughout life, but by the age of 18, 50% are free of tics

Etiology:

- The condition appears to be genetic
- There appears to be an autosomal dominant mode of inheritance
- 70% penetrance in women, 99% in men → explains why the condition is found more often in men
- DLGAP3 gene is a candidate gene
- Also associated with obsessive-compulsive disorder and attention deficit hyperactivity disorder

Pathophysiology:

- A disorder that involves neurotransmission in the basal ganglia and inferior frontal cortex
- No brain structural lesions
- Low levels of glutamate in the globus pallidus and low levels of cAMP in the cortex

Diagnostic Criteria:

Tics are sudden, rapid, recurrent nonrhythmic stereotyped motor or vocal symptoms.

DSM-5 diagnostic criteria for Tourette syndrome are as follows:

A. Multiple motor and one or more vocal tics have been present for some time during the illness
    1. Motor tics: eye blinking, head jerking, nose twitching, facial grimacing, shoulder shrugging, and mouth movements
    2. Vocal tics: throat clearing, grunting, sniffing, and coughing

B. The tics occur many times during a day, nearly every day, or intermittently over a year with no tic-free period more than 3 consecutive months
C. Age at onset < 18 years
D. The disturbance is not due to effects of a stimulant or a medical condition such as Huntington disease or post-viral encephalitis

Coprolalia which is involuntary obscene speech (40% of patients and is not part of the criteria)

Treatment:

- Psychoeducation
- Behavioral therapy

Patients with more severe and persistent tics

- Haloperidol or fluphenazine
- Tetrabenazine
- Alpha-2 agonists such as clonidine
- Atypical antipsychotics

References:

- First-Aid 2018

Pervasive Developmental Disorders:

Outline:

- Definition
- Autism Spectrum Disorder
- Asperger Syndrome
- Rett Syndrome
- Childhood Disintegrative Disorder
- References

Definition:

This is a diagnostic category that refers to a group of disorders that are characterized by delays in development of multiple basic functions related to socialization and communication. They include all autism spectrum disorders and Rett syndrome.

Autism Spectrum Disorder:

This disorder is characterized by poor social interactions, deficits in social communication, repetitive behaviors and restricted interests. For the diagnosis to be made, the symptoms' onset must be in early childhood. More common in boys. While most affected individuals have some sort of intellectual disability, a few can have unusual abilities (savants).

DSM-5 criteria are used to diagnose autism spectrum disorder.

Diagnostic criteria:

A. Persistent deficits in social communication and social interaction, for example:
    1. Deficits in social-emotional reciprocity: reduced sharing of interests and emotions, failure to initiate or respond to social interactions, and failure of normal back-and-forth conversation
    2. Deficits in nonverbal communicative behaviors such as maintaining eye-contact
    3. Deficits in developing, maintaining and understanding relationships
B. Restricted and repetitive patterns of behavior with at least two of the following:
    1. Stereotyped motor movements
    2. Insistence on sameness
    3. Highly restricted and fixated interest
    4. Hyper or hypo-reactivity to sensory input
C. Symptoms must be present in early childhood
D. Symptoms cannot be explained by intellectual disability or global developmental delay

Asperger Syndrome:

This diagnosis has been removed from the DSM-5 manual as it is now part of the autism spectrum disorder. The DSM-IV diagnostic criteria can be used to define what is meant by Asperger syndrome.

Diagnostic criteria:

A. Impairment in social interaction characterized by at least two of the following:
    1. Marked impairment in nonverbal communicative behaviors

2. Failure to develop or maintain peer relationships
3. Lack of spontaneous seeking to share enjoyment with other people
4. Lack of social and emotional reciprocity

B. Restricted and repetitive patterns of behavior with one or more of the following:
    1. Preoccupation with one or more stereotyped pattern of interest
    2. Inflexible adherence to specific routines and rituals
    3. Repetitive motor movements
    4. Preoccupation with parts of objects
C. The disturbance causes clinically significant impairment in social, occupational or other important areas of functioning
D. No delay in language development
E. No significant delay in cognitive development other than social interaction
F. Criteria are not met for another psychiatric disorder

Difference from autism:

- In autism, other cognitive developmental deficits and language deficits are present

Rett Syndrome:

After the recent understanding of the molecular mechanisms of Rett syndrome, it was removed from the category pervasive developmental disorders. The current understanding of Rett syndrome agrees that autistic features are present in the disease just like you would expect in fragile-X or Down syndrome, but this is explained by medical cause and is therefore not an autism spectrum disorder. Onset of symptoms is typically after the first year of life to four years.

Diagnostic criteria:

A. A positive test showing a MECP2 mutation (X-chromosome)
B. All the following symptoms:
    1. Decreased or loss of fine motor skills (cannot use hands to play with toys)
    2. Decreased or loss of verbal speech
    3. Abnormal gait
    4. Repetitive hand movements (wringing, squeezing, or clapping)
C. None of the following:
    1. Traumatic brain injury, neurometabolic disease, or severe CNS infection
    2. Abnormal psychomotor development during the first six months of life

Patients are typically females (x-linked) and the following symptoms can also occur but are not needed for the diagnosis:

- Breathing disturbances
- Impaired sleep pattern
- Abnormal muscle tone → often mistakenly diagnosed as cerebral palsy
- Scoliosis or kyphosis
- Intellectual disability
- Growth retardation

Childhood Disintegrative Disorder:

This disorder was removed from DSM-5 as it is now considered as part of the autism spectrum disorders. However, the DSM-4 diagnostic criteria can be used to define this disorder.

Diagnostic criteria:

A. Normal development for the first 2 years of life with normal verbal and nonverbal communication
B. Significant loss of previously acquired skills before the age of 10 years, manifested by at least two of the following:
    1. Deficits in expressive or receptive language
    2. Deficits in social skills or adaptive behavior
    3. Deficits in bowel or bladder control
    4. Deficits in ability to play with others
    5. Deficits in motor skills
C. Abnormal functioning in two or more of the following areas:
    1. Social interaction and nonverbal communication
    2. Verbal communication
    3. Restricted, repetitive and stereotyped patterns of behavior, interests, and motor mannerisms
D. The disturbance is not explained better by another pervasive developmental disorder or schizophrenia

Rationale of removing Asperger and childhood disintegrative disorder from DSM-5:

- You can notice the similarity in the symptoms of these three disorders
- The current understanding is that autism, Asperger, and childhood disintegrative disorder are the same disorder but with different degrees of severity
- Accordingly, the collective diagnosis “autism spectrum disorder” was introduced

References:

- First-Aid 2018

Schizophrenia Spectrum and Other Psychotic Disorders:

Outline:

Important Definitions Related to Psychosis:

Psychosis:

A period where perception of reality is distorted by delusions, hallucinations and other types of disorganized thought. Psychosis can occur in psychiatric illness and also in organic medical conditions.

Delusions:

These are unique, false and fixed idiosyncratic beliefs that cannot be shaken off despite evidence of being false and are not part of the patient's culture or religion. Grandiose, jealous, or persecutory delusions are some examples.

Disorganized thought:

The process of thought is disorganized, and this results in incoherent speech "word salad", or the speech can have loss of association.

Hallucinations:

These are defined as perceptions or experiences in the absence of external stimuli. Illusions are misperceptions of external stimuli. Examples:

- Visual – more common in medical illness
- Auditory – more common in psychiatric illness
- Olfactory – seen in temporal lobe epilepsy
- Gustatory – epilepsy
- Tactile – seen in alcohol or stimulant withdrawal

Schizophrenia:

This is a chronic mental illness that has distinct periods of psychosis and abnormal behavior and thought. This should result in a decline in functioning lasting six months or more.

The condition is associated with increased dopaminergic activity and decreased dendritic branching.

Epidemiology:

- More frequent in cannabis users
- Life-time prevalence is 1.5%
- More common in males
- Earlier presentation in men (in the 20s in men, while in the 30s in women)

Diagnostic criteria:

- Presence of two or more of the following for one month or more with at least one symptom from the first three:
    - Delusions
    - Hallucinations
    - Disorganized speech
    - Disorganized or catatonic behavior
    - Negative symptoms

The first four of these symptoms are considered as positive symptoms. Negative symptoms include:

- Affective flattening
- Avolition
- Asociality
- Alogia
- Anhedonia

Other features:

- Brain MRI might reveal ventriculomegaly
- Increased risk of suicide

Treatment:

- First-line treatment is atypical antipsychotics such as risperidone
- First generation typical antipsychotics can be used for positive symptoms:
    - Haloperidol
    - Thiazine and chlorpromazine
- Negative symptoms show little response to treatment, however atypical antipsychotics might alleviate them:
    - Ziprasidone
    - Risperidone
    - Olanzapine
    - Clozapine

Brief Psychotic Disorder:

- One or more positive symptom lasting for less than one month in a patient under stress
- Total duration of decline in functioning is less than one month

Schizophreniform Disorder:

- Same as schizophrenia but the total duration of decline in functioning is less than six months

Schizoaffective Disorder:

- Meets the diagnostic criteria of schizophrenia
- Meets the diagnostic criteria of major depressive or bipolar disorder
- Patients have solely psychotic symptoms (without a major mood episode) for more than 2 weeks

Delusional Disorder:

- A fixed, persistent and false belief system lasting for more than one month without any other functional impairments
- Can be shared by individuals in close relationships “shared delusional disorder”

Mood Disorder with Psychotic Features:

- Meets diagnostic criteria of major depressive disorder or bipolar disorder type 1
- Brief period of psychotic symptoms < 2 weeks with a major mood episode

Other Psychotic Disorders:

Schizoid personality disorder:

- Lack of interest and detachment from social relationships, apathy and restricted emotional expression

Schizotypal personality disorder:

- Extreme discomfort interacting socially, distorted cognitions or perceptions, strange beliefs and magical thinking

References:

- First-Aid 2018

Mood Disorders:

Outline:

- Definition
- Mood episodes
- Major depressive disorder
- Bipolar disorders
- Adjustment disorder
- References

Definition:

A mood disorder is characterized by an abnormal range of mood and internal emotional states with loss of control over them. These abnormal moods and emotional states need to cause impairment in social and occupational functioning.

Mood Episodes:

Depression episode: at least five and lasting for two weeks or more

- Depressed mood
- Sleep disturbance
- Loss of interest (anhedonia)
- Guilt
- Energy loss
- Concentration problems
- Appetite changes
- Psychomotor retardation
- Suicidal ideation

Manic episode: at least three, lasting for one week or more, and causes marked functional impairment and often hospitalization

- Distractibility
- Impulsivity
- Grandiosity
- Flight of ideas – not loss of association
- Psychomotor agitation
- Decreased need for sleep
- Pressured speech

Hypomanic episode:

Similar to a manic episode, but with less severe symptoms that do not impair social and occupational functioning severely. Lasts for 4 days or more

Major Depressive Disorder:

Diagnostic criteria:

- A depression episode that has five symptoms or more from the previous list
- Must have depressed mood or anhedonia
- For at least 2 weeks
- Not attributable to other medical conditions or substances

Treatment:

- Psychotherapy
- Selective-serotonin-reuptake inhibitors
- serotonin-norepinephrine-reuptake inhibitors
- MAO inhibitors
- Tricyclic antidepressants
- Electroconvulsive therapy in refractory cases

Persistent depressive disorder (dysthymia):

- Milder than major depressive disorder
- Two or more depression symptoms lasting for two years or more
- No more than two months without depressive symptoms

Bipolar Disorders:

Bipolar I:

One episode of mania with or without (a hypomanic or a depressive episode).

Bipolar II:

At least one episode of hypomania and one episode of depression plus no history of manic episodes

Cyclothymic disorder:

Alternating periods between hypomanic symptoms and depressive symptoms without meeting criteria for hypomanic episode or depressive episode that persists for two years or more. Treated with cognitive behavioral therapy, lithium and atypical antipsychotics.

Treatment:

- Mood stabilizers such as lithium or valproate
- Lamotrigine
- Atypical psychotics for an acute manic episode
- Patient's mood often normalizes between episodes

Adjustment Disorder:

- Mood and anxiety symptoms less than 3 months after a stressor
- Resolves within 6 months
- Treat with psychotherapy and medications for insomnia or nausea if prominent

References:

- First-Aid 2018

Bipolar Disorders:

Outline:

- Definition
- Epidemiology
- Manic episode
- Hypomanic episode
- Diagnostic criteria
- Treatment
- References

Definition:

Distinct period of abnormal and persistent elevated, expansive and irritable mood with increased activity and lasting for 1 weeks or more occur in bipolar disorders.

Epidemiology:

- Prevalence of 3.7%
- Typical onset between 18 and 44 years
- More than half of the patients do not seek medical help within the first five years of onset of symptoms
- The diagnosis was made 8 years in average after the onset of symptoms
- Equal frequency in males and females
- Age of onset in bipolar II is slightly higher (22) than that of bipolar I (18)

Manic Episode:

A. At least three of the following symptoms, or any number of symptoms that require hospitalization; and duration of symptoms lasting $\geq$ 1 week:
    1. Distractibility
    2. Impulsivity – patients seek pleasure without regard to consequences (hedonistic)
    3. Grandiosity – inflated self-esteem
    4. Flight of ideas where the thoughts are described as racing in their mind
    5. Increased activity or psychomotor agitation
    6. Decreased need for sleep
    7. Talkativeness and pressured speech
B. The symptoms should result in significant impairment of social or occupational functioning, or require hospitalization

Hypomanic Episode:

A. At least three of the following symptoms with a duration of symptoms lasting $\geq$ 4 consecutive days
    1. Distractibility
    2. Impulsivity – patients seek pleasure without regard to consequences (hedonistic)
    3. Grandiosity – inflated self-esteem
    4. Flight of ideas where the thoughts are described as racing in their mind

5. Increased activity or psychomotor agitation
6. Decreased need for sleep
7. Talkativeness and pressured speech

B. The symptoms must **not** lead to severe impairment in social and occupational functioning, or require hospitalization

Diagnostic Criteria:

Bipolar I:

- Presence of at least 1 manic episode, with or without a hypomanic or depressive episode
- The episodes can be separated by any length of time

Bipolar II:

- Presence of a hypomanic episode and a depressive episode
- Never had a manic episode

Treatment:

Psychotherapy in addition to mood stabilizers and atypical antipsychotics.

Mood stabilizers:

- Lithium:
  - Recommended in patients with manic euphoric, mild, moderate or severe episodes
  - Side effects:
    - Nephrogenic diabetes insipidus → block ADH receptors
    - Hypothyroidism → decreased free T_4 and T_3 | elevated TSH
    - If taken during pregnancy → Ebstein anomaly
- Valproic acid:
  - Recommended in patients with severe manic episodes or in patients with rapid cycling manic episodes
  - Side effects:
    - If taken during pregnancy → neural tube defects such as spina bifida
- Carbamazepine:
  - Can cause agranulocytosis

Atypical antipsychotics:

- Clozapine

References:

- First-Aid 2018

Major Depressive Disorder:

Outline:

- Depressive episode
- Major depressive disorder
- Other types of depression disorders
- Treatment
- References

Depressive Episode:

A. At least five of the following symptoms, symptoms must include either depressed mood or anhedonia or both; and duration of symptoms lasting ≥ 2 week:
    1. Depressed mood
    2. Sleep disturbance
    3. Loss of interest (anhedonia)
    4. Guilt
    5. Energy loss
    6. Concentration problems
    7. Appetite changes
    8. Psychomotor retardation
    9. Suicidal ideation

Sleep disturbances in a depressive episode include:

- Decreased rapid-eye-movement latency
- Increased rapid-eye-movement in the early phase of the sleep cycle
- Increased total duration of rapid-eye-movement sleep
- Repeated nighttime awakenings
- Early-morning awakening → terminal insomnia
- On EEG: decreased slow-wave sleep
- For more information about sleep physiology, please go to Neurology – Sleep Physiology

Major Depressive Disorder:

A. A major depressive episode that meets the criteria described above
B. The symptoms should result in significant impairment of social or occupational functioning
C. The patient should not have a history of a manic episode → reclassified as bipolar I
D. The symptoms cannot be explained by another medical or mental illness

Other Types of Depression Disorders:

Persistent depressive disorder:

A. Also known as dysthymia
B. Milder than major depressive disorder
C. Two or more depressive symptoms
D. Lasting for two years or more
E. No more than two months without depressive symptoms

Major depressive disorder with seasonal pattern:

A. Lasting two years or more
B. Two or more major depressive episodes associated with a seasonal pattern (e.g. winter)
C. Atypical symptoms are common, and they include hypersomnia, hyperphagia, and leaden paralysis

Depression with atypical features:

A. Mood reactivity (improved mood in response to positive events but briefly)
B. Hypersomnia and hyperphagia
C. Leaden paralysis
D. Long-standing interpersonal rejection sensitivity
E. Most common subtype of depression

Treatment:

Definitions related to response to treatment in depressive disorders:

- Recovery is remission and return to normal function
- Response is a reduction in 50% or more in the symptoms of major depressive disorder
- No response is a reduction less than 20% in the symptoms of major depressive disorder

First-line treatments:

- Cognitive behavioral therapy with an SSRI, SNRI (venlafaxine), bupropion, mirtazapine or agomelatine
- For severe depression SSRIs and SNRIs are more important than cognitive behavioral therapy, however psychotherapy is still needed

Severe major depression with psychotic features:

- An antidepressant combined with an antipsychotic
- Electroconvulsive therapy can be considered
- Tricyclic antidepressants plus an antipsychotic is a common regimen

Final goals:

- Once pharmacotherapy is started, assess fortnightly
- Re-evaluate at 4 weeks:
    - Remission → continue using same drug
    - Partial response → increase dose
    - No response → switch to a different class of antidepressants or consider electroconvulsive therapy

References:

- First-Aid 2018

Panic Disorder:

Outline:

- Definition
- Epidemiology
- Panic attacks
- Diagnostic criteria
- Treatment
- References

Definition:

Panic disorder is characterized by recurrent unexpected panic attacks that are followed by one month or more of persistent concern about having additional attacks or worry about the implications of having a future attack or a significant change in behavior related to the attacks.

Epidemiology:

- Prevalence of 2.2%
- Typical onset between 20 and 29 years
- Higher risk in females
- 25% also have agoraphobia
- Increased risk of developing major depressive disorder
- Increased risk of suicide
- Family history is a risk factor – possible role of genetics

Panic Attacks:

A. Periods of intense fear and discomfort that peak in 10 minutes and have $\geq$ 4 of the following features:
    1. Palpitations
    2. Paresthesia
    3. Depersonalization
    4. Derealization
    5. Abdominal distress
    6. Nausea
    7. Intense fear of dying
    8. Intense fear of losing control
    9. Light-headedness
    10. Chest pain
    11. Chills
    12. Chocking
    13. Sweating
    14. Shaking
    15. Shortness of breath

Diagnostic Criteria:

A. Occurrence of a panic attack that is not triggered followed by $\geq$ 1 month of $\geq$ 1 of the following:
    1. Persistent concern about future attacks
    2. Worrying about the consequences and implications of an attack
    3. Behavioral change related to the attacks

Diagnostic criteria of agoraphobia which is common in patients with panic disorder:

A. Anxiety about being in places or situations where escape might be difficult
B. Avoidance of situations and places that meet criterion A
C. Symptoms not better accounted for by substance abuse, another medical or mental disorder

Treatment:

First-line:

- Cognitive behavioral therapy
- SSRIs
- SNRIs such as venlafaxine

Acute panic attack treatment:

- Benzodiazepines → facilitate GABA by binding to $GABA_A$ receptors
- Potent anxiolytics

References:

- First-Aid 2018

Anxiety Disorders:

Outline:

- Generalized anxiety disorder
- Specific phobias
- Obsessive-compulsive disorder
- Post-traumatic stress disorder
- Treatment algorithm
- References

Generalized Anxiety Disorder:

- More common in women
- Life-time prevalence is 5 to 10%

Diagnosis:

A. Symptoms of anxiety lasting > 6 months
B. Unrelated to a specific person, situation or event
C. Associated with restlessness, irritability, sleep disturbance, fatigue, muscle tension, or difficulty concentrating
D. If the symptoms occur in response to an identifiable stressor that happened within 3 months and last < 6 months → adjustment disorder

Treatment:

First-line treatments:

- Cognitive behavioral therapy or medication
- Medications include SSRIs and SNRIs

Second-line treatments:

- Buspirone
- Tricyclic antidepressants
- Benzodiazepines

Risk of rebound anxiety upon discontinuation of medication.

Specific Phobias:

- More common in women
- Life-time prevalence is 10%

Diagnosis:

- Severe and persistent ≥ 6 months fear or anxiety due to the presence of a specific object or situation
- Fear is out of proportion to imminent threat
- The symptoms interfere with daily activities

- Exposure to the stimulus induces immediate fear, whereas, removing the stimulus reduces anxiety
- Social anxiety disorder is excessive fear of embarrassment in social situations such as public speaking or using public restrooms

Treatment:

- Systematic desensitization
- Cognitive behavioral therapy
- SSRIs or SNRIs such as venlafaxine

Treatment of performance type social anxiety disorder:

- Beta-blockers or benzodiazepines when needed

Obsessive-Compulsive Disorder:

- Equal frequency in males and females
- Lifetime prevalence is 3%
- Associated with other anxiety disorders, tic disorders, and especially Tourette syndrome

Diagnosis:

- Obsessions which are recurrent thoughts that persist despite trying to ignore
- Compulsions which are the actions "rituals" one take to reduce the anxiety that they might develop as a result of their obsessions

Treatment:

- Cognitive behavioral therapy
- SSRIs or SNRIs such as venlafaxine
- Clomipramine

Body dysmorphic disorder:

- The preoccupation with minor or imagined defect in appearance that results in significant emotional distress and impaired functioning
- Patients often seek cosmetic treatment
- The condition is treated with cognitive behavioral therapy

Post-Traumatic Stress Disorder:

Diagnosis:

- The patient experiences a life-threatening situation then develop any of the following:
    - Persistent hyperarousal
    - Avoidance of associated stimuli
    - Intrusive re-experiencing of the event in the form of nightmares or flashbacks
    - Changes in cognition or mood (horror or distress)
- The disturbance must last for more than one month and cause significant distress in social and occupational functioning
- Acute stress disorder lasts between 3 days and 1 month

Treatment:

- Cognitive behavioral therapy, SSRIs, or an SNRI (venlafaxine)
- Prazosin → reduces nightmares
- Acute stress disorder does not require pharmacotherapy

Treatment Algorithm:

- Multistep approach in the treatment to avoid polypharmacy

Step 1:

- The diagnosis of an anxiety disorder has been made
- Prescribe either an SSRI | NSRI, or, CBT

Evaluate the patient to look for full response → if yes, continue same treatment

Step 2:

- The patient did not fully respond to step 1
- Augment treatment chosen in step 1 use combined therapy (CBT + Medication)

Step 3:

- If the patient still does not show full response, use one of the following options:
    - Used combined pharmacotherapy or add benzodiazepines
    - Repetitive TMS, ECT, or vagal nerve stimulation

References:

- First-Aid 2018
- Bystritsky A, Khalsa SS, Cameron ME, Schiffman J. Current Diagnosis and Treatment of Anxiety Disorders. Pharmacy and Therapeutics. 2013;38(1):30-57.

Mental Status Examination:

Outline:

- Definition
- General Observations:
    - Appearance and behavior:
        - Appearance
        - Behavior
        - Eye contact
    - Mood and Affect
    - Motor activity:
        - Facial expressions
        - Movements
- Cognitive Functioning:
    - Attention
    - Executive functioning
    - Gnosia
    - Language
    - Memory
    - Orientation
    - Thought content
    - Thought process
    - Visuospatial proficiency
- Insight
- Judgement
- Mini-mental status examination
- References

Definition:

The mental status examination is a tool used in the assessment of systemic, neurologic and psychiatric disorders such as delirium, dementia, bipolar disorder or schizophrenia. A mini-mental status examination is a relatively brief version of the complete mental status examination. A mental status examination is not a neuropsychological evaluation, the latter being highly detailed and time-consuming.

General Observations:

The mental status examination has two main categories of components: general observations and cognitive functioning.

Appearance and Behavior:

The body habitus, eye contact, interpersonal style and style of dress are noted.

Appearance:

- Attention to detail
- Comment on attire, scars, tattoos, grooming and hygiene

Behavior:

- Observe the patient and comment if the patient is candid, congenial, cooperative, defensive, engaging, guarded, hostile, irritable, open, relaxed, resistant, shy, or withdrawn

Eye Contact:

- Comment on whether the patient can make good eye contact, or is it fleeting or sporadic. Note if there is no eye contact

Example of abnormalities in appearance and behavior:

- An irritable patient might have anxiety
- A paranoid patient could have a psychotic disorder
- Those who make poor eye contact could have depression or a psychotic disorder

Mood and Affect:

Mood:

This is the subjective report of the inner emotional state by the patient using his/her own words

You can ask a direct open-ended question “how is your mood?”

Affect:

This is the objective observation of the patient’s emotional state by the psychiatrist or medical doctor.

- Neutral, euthymic, dysphoric, apathetic, inappropriate

Motor Activity:

Facial Expressions:

Notice the range of emotions the patient is expressing with his/her face.

- Flat, blunted, restricted, full or normal, labile or expansive
- Congruence with reported mood by the patient

Movements:

- Akathisia:
  Excessive motor activity such as pacing, wringing of hands, or inability to sit still
- Bradykinesia:
  Psychomotor retardation which can be seen in depression, or a symptom of a physical disease (Parkinson’s disease)
- Catatonia:
  Immobility with muscular rigidity

Example of abnormalities in motor activity:

- Akathisia might be seen in anxiety, mood disorders, PTSD, or schizophrenia
- Bradykinesia might be seen in depression or Parkinson’s disease
- Catatonia is seen in patients with schizophrenia, severe depression and other psychotic disorders

Cognitive Functioning:

Attention:

Ability to focus on internal or external priorities. The patient can be asked to count by sevens or fives.

Example of abnormalities in attention:

- Could have deficits in ADHD, delirium, dementia, mood disorders, or psychotic disorders

Executive Functioning:

The ordering and implementation of cognitive functions necessary to perform appropriate behaviors. The patient could be asked to draw a clock with hands set to 10:30 or to alternate numbers with letters in ascending order.

Example of abnormalities in executive functioning:

- Impaired in delirium, dementia, mood disorders, and stroke

Gnosia:

The ability to name common objects and their function.

Example of abnormalities in gnosia:

- Temporal lobe epilepsy, advanced dementia, or stroke

Language:

Check the quality of speech not the content:

- Appropriateness of speech
- Rate of speech (> 100 words per minute is normal, < 50 words per minute is abnormal)
- Appropriate for education level

Example of abnormalities in language and speech:

- Rapid and pressured speech in mania
- Slow or impoverished speech in delirium, depression and schizophrenia
- Inappropriate conversation in schizophrenia
- Inappropriate for education level in dementia, depression, or stroke

Memory:

The recall of past events. Can be classified not declarative and procedural. Procedural memory is the ability to complete a learned task without conscious thought.

- Declarative memory can be tested with a simple question such as when is your birthday
- Ask the patient to repeat three words immediately and then again in five minutes to test declarative memory
- Ask the patient to sign his or her name while answering unrelated questions to test procedural memory

Example of abnormalities in memory:

- Long-term deficits are seen in advanced dementia, amnesia, dissociative disorder, and previous stroke

- Short-term deficits are seen in ADHD, dementia, inattention or substance abuse

Orientation:

The ability of the patient to recognize his place in relation to time and space. Orientation to time, space and person is tested.

- Questions about what year or month is it, what city/building or floor are you in, what is your name, and when were you born?

Example of abnormalities in orientation:

- Head trauma
- Amnesia, delirium, dementia, mania, stroke, severe depression

Thought Content:

Here, you try to identify what the patient is thinking in terms of delusions, hallucinations, homicidal ideation, obsessions, phobias and suicidality.

- Ask about thoughts or images that the patient cannot get out of his/her head
- Excessive fears
- Whether they think people are trying to hurt them
- Whether they think people are talking behind their back
- Whether they think people are stealing from them
- Questions related to suicidal ideation: ask in this order:
    - Do you feel life is not worth living?
    - Have you ever thought about hurting yourself? If so, how would you do it?
    - Have you ever thought the world would be better off without you?
- Questions about hallucinations:
    - Do you see things that upset you?
    - Do you see, hear, smell or feel things that are not really there?
    - Have you ever heard something that other people could not?
- Have you ever thought about hurting others or getting even with those who have wronged you?

Example of abnormalities in thought content:

- Delusions can be seen in patients with mania, psychotic disorders, or major depressive disorder with psychotic features
- Hallucinations can be seen in patients with delirium, dementia, schizophrenia, or substance abuse
- Homicidal ideation can be seen in patients with mood, personality, or psychotic disorders
- Obsessions are seen in patients with OCD, PTSD, and psychotic disorder
- Phobias in specific phobic disorders
- Suicidality is seen in depression, PTSD and substance abuse

Thought Processes:

This domain is concerned with the organization of thoughts in a goal-oriented pattern.

Circumferential:

The patient goes through multiple related thoughts before arriving at the right answer for the question that was asked

Disorganized thoughts:

Patient moves from one topic to another without coherence or logic.

Tangential:

The patient avoids to answer the question by listening to the question and then begins discussing related thoughts but never answers the question.

Visuospatial Proficiency:

This test is more useful in medical conditions such as delirium, dementia and stroke. The patient is instructed to copy intersecting pentagons or a 3D cube on paper. It tests the patient's ability to perceive and manipulate objects in space.

Insight:

Does the patient understand and recognize his or her illness. The patient is inquired about his/her explanation of the current problem and his/her awareness about treatment options. Graded as good, fair or poor.

Judgement:

Tests the patient's ability to make sound and reasoned decisions. It is important because it can affect handling of treatment plan. Graded as good, fair or poor.

Mini-Mental Status Examination:

Only takes the following domains into account:

- Attention
- Language
- Memory
- Orientation
- Visuospatial proficiency

More appropriate for medical conditions rather than psychiatric disorders.

References:

- First-Aid 2018

Personality Disorders Clusters:

Outline:

- Cluster A personality disorders
- Cluster B personality disorders
- Cluster C personality disorders
- References

Cluster A Personality Disorders:

These individuals are described as odd or eccentric. They have problems in developing meaningful social relationships, however they do not have full-blown psychosis. Genetic predisposition to other psychotic disorders and schizophrenia.

Paranoid:

- Pervasive distrust (accusatory) of others
- Suspiciousness of others
- Very strong cynical view of the world

Schizoid:

- Voluntary withdrawal from social interactions (aloof)
- Limited emotional expression
- Prefers social isolation

Schizotypal:

- Eccentric appearance
- Odd beliefs and magical thinking
- Interpersonal awkwardness

Cluster B Personality Disorders:

These are dramatic and erratic emotional individuals that are at an increased risk of mood disorders and substance abuse.

Antisocial:

- More common in males
- Patient must be 18 years or older
- Must have history of conduct disorder before age 15
- Repeated violation of rights of others and rules, lack of remorse, and criminality

Borderline:

- More common in females
- Unstable mood which leads to unstable interpersonal relationships
- Impulsivity
- Self-mutilation
- Suicidal ideation or attempts

- Sense of emptiness

Histrionic:

- Excessive emotionality and excitability
- Attention seeking behavior
- Sexually provocative
- Overly concerned with appearance

Narcissistic:

- Grandiosity
- Sense of entitlement
- Does not empathize with others and requires excessive admiration
- Demands the best of others
- Reacts to criticism with anger and rage

Cluster C Personality Disorders:

These are individuals that are described as anxious and fearful. There is predisposition to anxiety disorders.

Avoidant:

- Hypersensitive to rejection
- Socially inhibited and timid
- Feelings of inadequacy
- Still, wants to be with others

Obsessive-compulsive:

- Preoccupation with control, and perfectionism
- Behavior consistent with one's own beliefs and attitudes

Dependent:

- Always need for support
- Low-self-esteem and confidence
- Tend to get stuck in abusive relationships

References:

- First-Aid 2018

Somatic Symptom Disorder:

Outline:

- Definitions of Somatic Symptom Disorder and Subclassifications
- Epidemiology of Somatic Symptom Disorder
- Pathophysiology of Somatic Symptom Disorder
- Treatment
- References

Definitions and Subclassifications:

Symptoms are physical and real to the patient; however they are unconscious. Motivation should be absent in a somatic symptom disorder, in contrast to factitious disorder or malingering. These conditions are more common in women (10:1 female to male ratio for somatic symptom disorder).

Somatic symptom disorder:

A. One or more somatic symptoms that cause significant distress and disruption in daily life
B. One or more excessive thoughts, feelings, or behaviors related to the somatic symptoms
C. Symptoms include pain, or fatigue and they should last for six months or more (six months of being symptomatic, but the same symptom does not have to last for six months)

Illness anxiety disorder:

A. Also known as hypochondriasis
B. Excessive preoccupation with acquiring or having a serious illness despite medical evaluation
C. Minimal somatic symptoms

Conversion disorder:

A. Somatic symptom disorder with prominent neurologic symptoms such as paralysis
B. Not compatible with any known neurologic medical condition

The condition often occurs following an acute stressor. Patients are aware of the nature of the symptoms, but are indifferent toward them. The condition is more common in adolescent and young adult females.

Malingering and factitious disorders are defined as follows:

Malingering:

A. Not a mental disorder
B. Symptoms are made up intentionally for an intentional motivation
C. The individual seeks specific gains
D. The individual might exaggerate an existing medical condition for the secondary gain
E. Complaints go away after gain

Factitious disorder:

A. Symptoms are intentional, but motivation is unconscious
B. The patient consciously creates the physical/psychological symptoms
C. The goal is to assume sick role to seek medical attention and sympathy

D. Mainly internal gain
E. When the condition results in multiple hospital admissions and willingness to go for invasive procedures → Munchausen syndrome | more common in females and healthcare workers
F. When the illness is caused by a caregiver in a child or an elderly → Munchausen syndrome by proxy → considered as form of child/elder abuse

Epidemiology of Somatic Symptom Disorder:

- Estimated prevalence is 0.1%
- Those who partially meet the diagnostic criteria of somatic symptom disorder can be as high as 11% of the general population
- The estimated prevalence of conversion disorder in psychiatric inpatient wards is 15%
- Symptoms should start in adolescence → onset of somatic symptoms in a patient who never had somatization issues before → search for an occult medical condition

Treatment:

- Regular office visits with the same physician to build a relationship in combination with psychotherapy
- Try to not treat the somatic symptoms as much as you can

References:

- First-Aid 2018

Eating Disorders:

Outline:

- Definition
- Anorexia nervosa
- Bulimia nervosa
- Binge eating disorder
- References

Definition:

Eating disorders are characterized by abnormal eating patterns which can have long-term impacts on the patient.

Anorexia Nervosa:

Epidemiology:

- Prevalence is 1%
- More common among young women and adolescent girls
- Poor prognosis

Diagnosis:

The DSM-5 diagnostic criteria for anorexia nervosa are the following:

A. Restriction of intake relative to requirements which result in a significantly low body weight which must be less than the minimal normal for the patient's age
B. Intense fear of gaining weight or becoming fat and persistent behavior that interferes with weight gain
C. Disturbance in the way in which one's body shape is perceived or experienced

The body mass index (BMI) is used to classify anorexia nervosa by severity:

- **Mild**: BMI $\geq$ 17 kg/m^2
- **Moderate**: BMI 16 – 16.99 kg/m^2
- **Severe**: BMI 15 – 15.99 kg/m^2
- **Extreme**: BMI < 15 kg/m^2

The following clinical findings and characteristics are seen in patients with anorexia nervosa:

- BMI is < 18.5
- Amenorrhea secondary to loss of pulsatile GnRH secretion
- Hypokalemia
- Hypophosphatemia
- Hypomagnesemia
- Bradycardia and arrhythmias secondary to hypokalemia
- Metabolic alkalosis
- Osteopenia which can be irreversible
- Restricting or binge-eating subtypes

Treatment:

- Psychotherapy, usually cognitive behavioral therapy
- Treatment of the physical symptoms
- Fluoxetine or other SSRIs for the treatment of comorbid depression or anxiety

Refeeding syndrome:

- Severely malnourished patients who start receiving energy intake suddenly might develop hyperinsulinemia
- The increased insulin secretion results in hypophosphatemia, hypokalemia and hypomagnesemia
- This can result in cardiac arrhythmias, rhabdomyolysis and seizures

Bulimia Nervosa:

Epidemiology:

- Higher prevalence than anorexia nervosa, 1.5%
- More common in women, aged 16 to 22 years
- Can be classified into binge-eating and non-purging types

Diagnosis:

The DSM-5 diagnostic criteria for bulimia nervosa are the following:

A. Recurrent episodes of binge eating. An episode of binge eating must include the following two characteristics:
    1. Eating large quantities of food in a small amount of time
    2. Lack of control over eating during the episode
B. Recurrent inappropriate compensatory behavior to prevent weight gain such as induced vomiting, use of laxatives, diuretics, fasting or excessive exercise
C. These two behaviors of binge eating, and compensatory behaviors occur at least once per week for three months
D. Self-evaluation is influenced by body shape and weight
E. Does not occur during episodes of anorexia nervosa

The patients have the following characteristics:

- BMI > 18.5 but less than 25
- Electrolyte disturbances similar to anorexia nervosa
- Russell signs:
  Calluses and abrasions on the dorsum of the hand caused by repeated contact with the incisors during self-induced vomiting
- Dental carries
- Enamel erosion from repeated acidic exposure to the teeth due to vomiting

Treatment:

- Cognitive behavioral therapy
- Fluoxetine or other SSRIs do help with bulimia nervosa symptoms
- SSRIs can be also used for comorbid symptoms such as anxiety and depression
- Avoid bupropion → can cause seizures

Binge-Eating Disorder:

Epidemiology:

- Prevalence > 3%
- Equal occurrence in men and women
- Prevalence among obese people is > 50%

Diagnosis:

The DSM-5 diagnostic criteria for bulimia nervosa are the following:

A. Recurrent episodes of binge eating. An episode of binge eating must include the following two characteristics:
    1. Eating large quantities of food in a small amount of time
    2. Lack of control over eating during the episode
B. The binge-eating episodes are associated with $\geq$ 3 of the following:
    1. Eating is more rapid than normal
    2. Eating does not stop until the patient is uncomfortably full
    3. Eating large amounts of food even when not hungry
    4. Eating alone because the patient feels embarrassed about how much he/she eats
    5. Feeling disgusted with oneself and guilty
C. Marked distress regarding binge eating
D. Occurs once per week or more for three months

Patients with binge-eating disorder are characterized by the following:

- Older than your typical bulimia nervosa or anorexia nervosa patients
- Binge-eating without compensatory behavior as in bulimia nervosa
- Complications related to obesity such as dyslipidemia and increased cardiovascular risk
- Limited ability to lose weight

Treatment:

- Cognitive behavioral therapy is first-line treatment
- Sibutramine can be used for weight loss
- Orlistat is also helpful
- SSRIs are used for comorbid depression or anxiety
- Lisdexamfetamine

References:

- First-Aid 2018
- Sim LA, McAlpine DE, Grothe KB, Himes SM, Cockerill RG, Clark MM. Identification and Treatment of Eating Disorders in the Primary Care Setting. Mayo Clinic Proceedings. 2010;85(8):746-751. doi:10.4065/mcp.2010.0070.

Stages of Change:

Outline:

- Definition and Theory
- Precontemplation
- Contemplation
- Preparation
- Action
- Maintenance
- Relapse
- References

Definition and Theory:

Psychologists and psychiatrists often deal with patients who are addicts. Understanding the different stages of change can help the psychiatrist in understanding his or her clients and offer the appropriate therapy or intervention.

A lot of research has been done on this topic which lead to the identification of five distinct stages of change. In fact, most addiction programs focus on the understanding of these stages of change in the first step in overcoming an addiction. These intentional behavior changes occur along a temporal dimension and involve cognitive and behavior components.

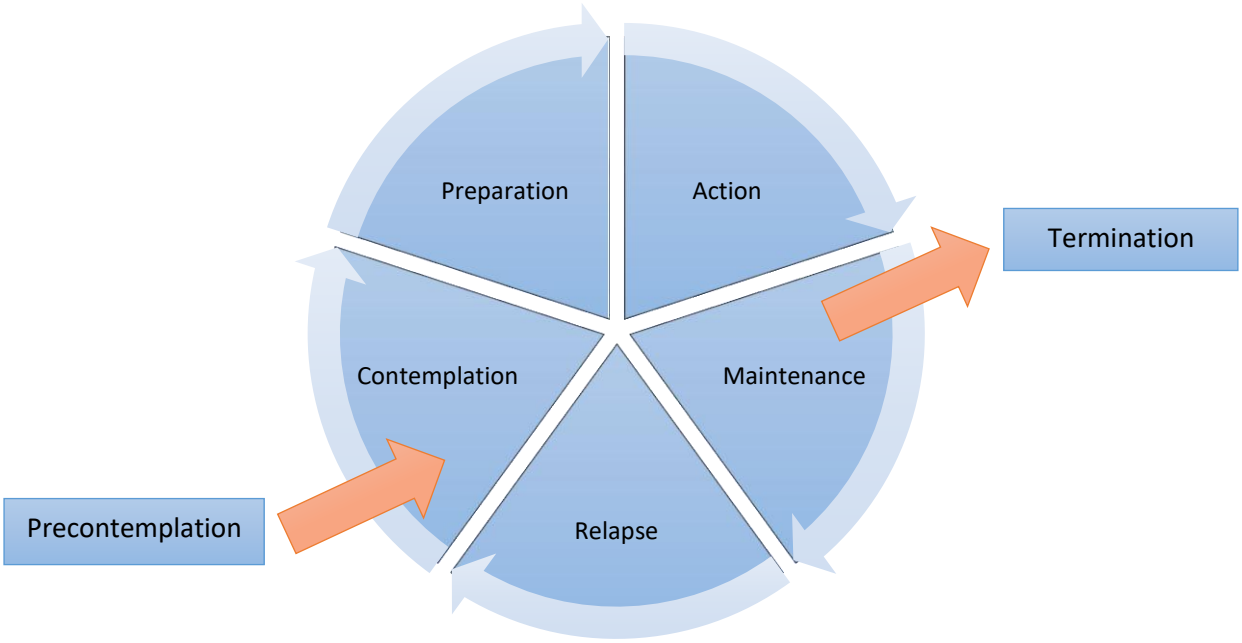

Figure 1: Stages of change. The goal of successful therapy of addiction is to go to termination instead of relapse after maintenance.

Precontemplation:

Definition:

The addict is not thinking seriously about change. They are not interested in help and they can rationalize and defend their bad habits. To them, there is no problem in the first place to start with.

Techniques:

- The goal of any intervention at this stage is to make the addict enter contemplation stage
- You should validate the lack of readiness
- It is important to assure them that the decision is theirs
- Encourage self-exploration
- Explain the risks of current behavior in a personalized approach

Contemplation:

Definition:

The patient becomes aware that there is a problem and they can understand the consequences of such bad habits. They might consider the possibility of changing but are still ambivalent about it. Patients might start saying this like they want to change, but not right away because they are not ready yet.

Techniques:

- The goal is to make the patient enter the preparation stage
- Validate the lack of readiness
- Again, clarify that the decision is theirs and they are not forced to do anything
- At this stage, it is important to use cognitive behavioral techniques and ask the patient to think of the pros and cons of behavior change
- Set new expectations and promote them in your future sessions

Preparation:

Definition:

The patient is finally ready to change. He or she are testing the waters of change and really consider changing within the next month.

Techniques:

- Use a reward system and appreciate the patient's readiness
- Identify the obstacles that the patient might face and solve them
- Help the patient to identify with social support groups and suggest addiction meetings or other types of support
- Encourage the patient to take small initials steps and not to expect to change in one night

Action:

Definition:

At this stage, the patient is already doing new behaviors and the old behaviors are dying out. The new, better, behavior lasts for three to six months in this stage. Willpower is important.

Techniques:

- This is a true milestone in the recovery of the addict, acknowledge that

- Your sessions should focus on cues and social support
- Encourage the patient to be confident and use self-efficacy in dealing with obstacles
- Patients tend to start experience feelings of loss, therefore it is important to remind them about the long-term benefits

Maintenance:

Definition:

The patient is still practicing the new behaviors and he/she is committed to change. This last from six months to multiple years, because there is always the risk of relapse. The goal is for the patient to reach termination where former bad behaviors are no longer perceived as desirable.

Techniques:

- Follow-up support
- Reinforce internal rewards
- Discussion of relapse and how to cope with it should be started

Relapse:

Definition:

Returning to old behaviors and abandoning new changes. This does not always happen but should be considered as part of the stages of change. If this happen, it just means we need to start over. It does not mean that the addict is weak, bad, or not up to the challenge.

Techniques:

- It is extremely important to identify the trigger for relapse
- Reassess the motivation of the patient. In some cases, you can help the patient to enter the contemplation stage without going through precontemplation again
- Plan stronger coping strategies to fight future urges and prevent relapses

References:

- First-Aid 2018
- http://www.cpe.vt.edu/gttc/presentations/8eStagesofChange.pdf

Psychoactive Drugs: Intoxication and Withdrawal:

Outline:

- Definitions
- CNS Depressants
- Opioids
- CNS Stimulants
- Hallucinogens
- References

Definitions:

Substance use disorder:

The patient has a compulsive pattern of drug use and this is driven by physical and psychological dependence.

Physical dependence:

Most psychoactive drugs result in physical changes in the brain neurotransmitter transmission systems. The sudden discontinuation of the psychoactive drug results in withdrawal symptoms that are physical.

Psychological dependence:

An emotional rather than a physical dependence on a psychoactive substance. The patient uses the drug to relieve psychological distress. Withdrawal symptoms are mild and more in the form of anxiety, depression or other psychiatric complaints.

Tolerance:

When physical dependence occurs, the patient will require more and more of the same drug to experience the effects previously seen at lower doses. Can lead to overdose.

Withdrawal:

A group of negative symptoms that are experienced by the patient who has physical dependence on a drug once the drug is discontinued.

The different classes of psychoactive drugs are shown in *Figure 1*. The discussion will be limited to the most important and common drugs.

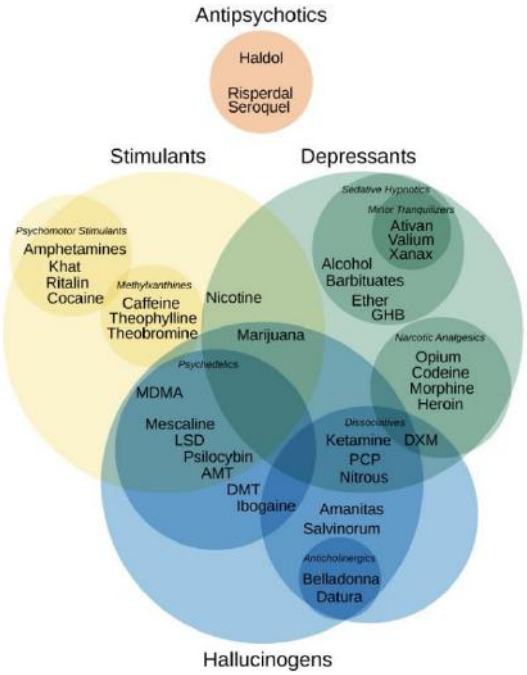

Figure 1: Classes of psychoactive drugs. Source: https://courses.lumenlearning.com/waymaker-psychology/chapter/reading-psychoactive-drugs/

CNS Depressants:

- CNS depressants include alcohol, barbiturates, and benzodiazepines
- They depress the CNS by working as agonists of $GABA_A$ receptors
- They can result in mood elevation, decreased anxiety, sedation, and behavioral disinhibition
- Respiratory depression

Alcohol:

- At low doses it can cause euphoria
- At larger doses it can cause sedation
- Decreased reaction time and visual acuity, level of alertness, and behavioral control
- It can cause emotional lability, slurred speech, ataxia, or coma
- Elevated serum GGT levels
- AST value is two times higher than ALT value
- Withdrawal:
    - 3 to 36 hours: tremors, insomnia and GI upset
    - 6 to 48 hours: withdrawal seizures
    - 12 to 48 hours: alcoholic hallucinosis which is often visual
    - 48 to 96 hours: delirium tremens
    - Treat with benzodiazepines

Barbiturates:

- Low safety margin → respiratory arrest
- When intoxicated, respiratory assistance is needed
- Withdrawal:
    - Delirium
    - Life-threatening cardiovascular collapse

Benzodiazepines:

- Greater safety margin than barbiturates
- Can cause ataxia and minor respiratory depression
- Treatment: flumazenil which is a benzodiazepine receptor antagonist → can cause seizures
- Withdrawal:
    - Sleep disturbances
    - Depression
    - Rebound anxiety
    - Seizures

Opioids:

- Include heroin, morphine, methadone, and codeine
- Extremely high potential for abuse
- Heroin can be snorted, smoked or injected intravenously

Intoxication:

- Euphoria
- Respiratory and CNS depression
- Decreased gag reflex
- Pinpoint pupils
- At very high doses, patients can develop seizures
- Treatment: naloxone | very short-half life and the patient might need repeated administration of naloxone

Withdrawal:

- Dilated pupils
- Piloerection
- Sweating
- Fever
- Rhinorrhea and lacrimation
- Yawning
- GI upset
- Treatment of addiction:
    - Long-term support with a treatment plan based on the five stages of change – see lecture Stages of Change
    - Methadone
    - Buprenorphine

CNS Stimulants:

- These include amphetamines, cocaine, and nicotine. Caffeine is a CNS stimulant as well
    - Cocaine blocks norepinephrine and DA reuptake
    - Amphetamines increase synaptic norepinephrine
    - Nicotine is an agonist of PNS and CNS cholinergic receptors
    - Caffeine enhances DA by blocking ADO receptors
- They cause mood elevation, psychomotor agitation and cardiac arrhythmias

- Anxiety and insomnia are common side effects

Amphetamines:

- Can cause euphoria and grandiosity
- Pupillary dilation
- Hypertension and tachycardia
- Anorexia
- Paranoia
- Fever
- Methamphetamine can cause skin excoriations
- In severe intoxication → cardiac arrest and seizures
- Benzodiazepines are indicated for the treatment of agitation and seizures

Cocaine:

- Like amphetamines but patients also have tactile hallucinations, angina, and sudden cardiac death
- Chronic use might lead to perforated nasal septum → from vasoconstriction
- Treatment is with alpha-blockers and benzodiazepines

Nicotine:

- Most tobacco products have nicotine
- It causes restlessness
- Withdrawal:
    - Irritability
    - Anxiety
    - Restlessness
    - Difficulty concentrating
    - Treat with nicotine patch/gum or bupropion/varenicline

Caffeine:

- Can cause restlessness, and increased diuresis
- Muscle twitching
- The most commonly used and abused CNS stimulant
- Withdrawal:
    - Headache
    - Difficulty concentration
    - Flu-like symptoms

Note: Addiction to these psychoactive drugs is common. Patients should be referred to addiction programs that are based on the stages of change that were discussed in the lecture "Stages of Change".

Hallucinogens:

- These include marijuana, synthetic cannabinoids, ecstasy, lysergic acid diethylamide, and phencyclidine
- They all result in profound alterations in sensory and perceptual experiences
    - Lysergic acid diethylamide (LSD) is a serotonin receptor agonist
    - Phencyclidine is an NMDA receptor antagonist
    - Marijuana has the active ingredient delta-5-tetrahydrocannabinol which binds to cannabinoid receptors → inhibition of adenylate cyclase → decreased cAMP production
- Less likely to result in abuse when compared to the previous psychoactive drugs

Marijuana:

- Can cause euphoria, anxiety, and paranoid delusions
- Perception of time slowness
- Impaired judgement
- Increased appetite
- Conjunctival injection
- Hallucinations
- Dronabinol is a pharmaceutical form that is used as an antiemetic in chemotherapy and an appetite stimulant in AIDs patients
- Withdrawal:
    - Irritability
    - Anxiety and insomnia
    - Depression
    - Decreased appetite

LSD:

- Also include psilocybin (shrooms) and mescaline (peyote)
- They work on the serotonin receptors in the limbic system, brainstem, and neocortex
- Distortion in the perception of reality (visual and auditory)
- Depersonalization
- Can cause anxiety, paranoia, and psychosis

Phencyclidine:

- Violence, impulsivity, and psychomotor agitation
- Nystagmus
- Tachycardia and hypertension
- Analgesia
- Psychosis, delirium and seizures
- Psychomotor agitation can be severe and lead to trauma
- Ketamine abuse also belongs to this category

References:

- First-Aid 2018
- https://courses.lumenlearning.com/waymaker-psychology/chapter/reading-psychoactive-drugs/

Typical Antipsychotics:

Outline:

- Neurotransmitter Derangements in Schizophrenia
- Typical Antipsychotics
- Phenothiazines and Butyrophenones
- Side Effects
- Neuroleptic Malignant Syndrome
- References

Neurotransmitter Derangements in Schizophrenia:

- In the 1950s and 1960s, it was populated that the pathogenesis of schizophrenia is caused by excess dopaminergic activity
- This led to the development of the first-generation typical antipsychotics which all work as D_2 receptor antagonists
- Now we know this is not entirely true and that other neurotransmitter systems are also affected in schizophrenia:
    - Glutamatergic system dysfunction
    - G-protein signaling abnormalities
    - Serotoninergic system abnormalities
- This led to the development of the atypical antipsychotics

Typical Antipsychotics:

- Their use was common before the 1990s
- Also known as neuroleptics because of their side-effects' profile
- Their mechanism of action is mainly D_2 receptor antagonism

Effects of typical antipsychotics on the main dopamine pathways:

<u>The mesolimbic pathway:</u>

- The inhibition of this pathway explains the antipsychotic effects of typical antipsychotics

<u>The nigrostriatal pathway:</u>

- The extrapyramidal symptoms of typical antipsychotics occur due to the inhibition of this pathway

<u>The tuberoinfundibular pathway:</u>

- Dopamine is a prolactin-inhibiting factor
- The inhibition of this pathway leads to hyperprolactinemia

<u>The mesocortical pathway:</u>

- This pathway is dysfunctional in schizophrenic patients
- Blockage of this pathway results in negative symptoms and cognitive deficits
- Because typical antipsychotics also inhibit this pathway, they do not help with the negative symptoms of schizophrenia

The positive symptoms of schizophrenia:

- Hallucinations
- Delusions
- Disorganized thought
- Catatonia

The negative symptoms of schizophrenia:

- Social withdrawal
- Loss of drive
- Diminished affect and flat faces
- Paucity of speech
- Impaired personal hygiene

Typical antipsychotics work on the positive symptoms of schizophrenia.

Phenothiazines and Butyrophenones:

These are the two classes of typical antipsychotics. The following table summarizes the differences between the two different classes.

	PHENOTHIAZINES	BUTYROPHENONES
EXAMPLES	Chlorpromazine, fluphenazine, and thioridazine	Haloperidol
MECHANISM OF ACTION	D_2 receptor antagonists	D_2 receptor antagonists
HALF-LIFE	Very long	Shorter
SEDATIVE POTENTIAL	Yes	No

Clinical uses:

- Schizophrenia
- Psychosis
- Acute manic episode
- Tourette's syndrome

Side Effects:

The following table summarizes the main side-effects of typical antipsychotics.

SIDE EFFECT	MECHANISM
ACUTE EXTRAPYRAMIDAL SYNDROMES	Dopamine blockade of the basal ganglia
SEDATION	Blockage of H_1 receptors
SKIN PIGMENTATION	Conversion of dopamine to melanin
TACHYCARDIA	Muscarinic receptor blockade
CONSTIPATION AND DRY MOUTH	Muscarinic receptor blockade
JAUNDICE	Bile duct obstruction in chlorpromazine

Acute extrapyramidal syndromes:

- Acute dystonia (muscle spasm, stiffness and oculogyric crisis
- Occurs in the first hours to days after the administration of typical antipsychotics
- Treated with benztropine or diphenhydramine

Subacute extrapyramidal syndromes:

- Occur days to months after starting typical antipsychotics
- Akathisia which is defined as restlessness and is treated with beta-blockers, benztropine or benzodiazepines
- Parkinsonism which is treated with amantadine or benztropine

Tardive dyskinesia:

- Chronic form of extrapyramidal syndromes
- Can occur months to years after being on typical antipsychotics
- Orofacial chorea
- The patient should be switched to atypical antipsychotics

Neuroleptic Malignant Syndrome:

Clinical findings:

- Hyperthermia
- Severe muscular rigidity → muscular damage (myoglobinuria and elevated CK)
- Autonomic instability (elevated blood pressure, tachycardia and tachypnea)
- Changing levels of consciousness (encephalopathy)
- Catatonia or stupor
- Can be fatal

Pathophysiology:

- Central dopamine blockade
- Blockade of dopamine receptors in the hypothalamus → hyperpyrexia, tachycardia and blood pressure instability
- Blockage of dopamine receptors in the basal ganglia → rigidity → muscle damage
- Direct effect of dopamine in the muscles → increased muscle cell metabolism → hyperpyrexia and rigidity
- Possible genetic predisposition

Treatment:

- Discontinue antipsychotics immediately
- Dantrolene is helpful (post-synaptic muscle relaxant → inhibits the release of calcium from the sarcoplasmic reticulum)
- Bromocriptine and other dopamine agonists

References:

- First-Aid 2018
- http://www.rroij.com/open-access/first-generation-antipsychotics-pharmacokinetics-pharmacodynamicstherapeutic-effects-and-side-effects-a-review-.pdf

Atypical Antipsychotics:

Outline:

- Overview
- Efficacy
- Targeted receptors
- Clinical use
- Side effects
- References

Overview:

Typical antipsychotics have many limitations:

- Up to one third of patients do not respond
- Limited efficacy against negative symptoms
- High risk of relapse
- Severe side effects related to extrapyramidal syndromes
- Significant safety issues related to neuroleptic malignant syndrome

This, and the new advances in the understanding of the pathophysiology of schizophrenia and psychotic disorders, led to the development of new "atypical" antipsychotics.

Atypical antipsychotics are superior to typical antipsychotics in the following regards:

- Increased efficacy against positive symptoms, especially in drug-resistant patients
- Efficacy against negative symptoms of schizophrenia
- Decreased risk of acute extrapyramidal syndromes such as parkinsonian, dyskinesias, and akathisia
- Decreased risk of tardive dyskinesia
- Decreased risk of hyperprolactinemia

They include clozapine, risperidone, olanzapine, sertindole, quetiapine, aripiprazole, and ziprasidone.

Efficacy of atypical antipsychotics:

- Up to 85% of patients respond
- Help up to half of those who did not respond to typical antipsychotics
- Reduce relapse rate to less than 15%

Targeted Receptors:

They can be classified into MARTA, SDA, selective D_2/D_3 antagonists and partial dopamine agonists.

MARTA:

- Multi-acting receptor targeted agents
- **Clozapine**: serotonin, alpha-1, histamine-1, and muscarinic receptors antagonist
- **Quetiapine**: alpha-1 and histamine-1 receptor antagonist

- **Olanzapine**: serotonin, D_2, alpha-1, muscarinic, and histamine-1 receptor antagonists

SDA:

- Serotonin-dopamine antagonists
- Risperidone, ziprasidone, and sertindole

Selective D_2/D_3 antagonists:

- Sulpiride
- Amisulpiride

Partial dopamine agonists:

- Aripiprazole

Clinical Use:

- Schizophrenia – positive and negative symptoms
- Bipolar disorder, OCD, anxiety disorder, depression, mania and Tourette syndrome
- Clozapine is indicated in patients with drug-resistant schizophrenia

Side Effects:

- QT interval prolongation
- Extrapyramidal syndromes (but much less common than with typical antipsychotics)
- Olanzapine and clozapine can cause metabolic syndrome (obesity, diabetes and hyperlipidemia)
- Clozapine can cause agranulocytosis and seizures
- Risperidone is associated with hyperprolactinemia → amenorrhea, galactorrhea and gynecomastia

References:

- First-Aid 2018

Neurotransmission in Depression:

Outline:

- Definition of Major Depressive Disorder
- The Serotonin Synapse
- The Direct Effects of Antidepressants
- The Early Effects of Antidepressants
- The Long-term Effects of Antidepressants
- References

Definition of Major Depressive Disorder:

Patients with major depressive disorder have a major depressive episode for more than two weeks that results in significant impairment of social and occupational functioning and is characterized by at least five of the following where the first or the second symptom is a prerequisite for diagnosis:

- Depressed mode
- Anhedonia
- Sleep disturbances
- Guilt
- Energy loss
- Concentration problems
- Appetite changes
- Psychomotor retardation
- Suicidal ideation

The Serotonin Synapse:

The previous and most studied understanding of the pathogenesis of depression and depressive disorders focused on serotonin system dysfunction. Understanding the different steps involved in serotonin synthesis, release, reuptake and breakdown clarifies the mechanism of action of antidepressants.

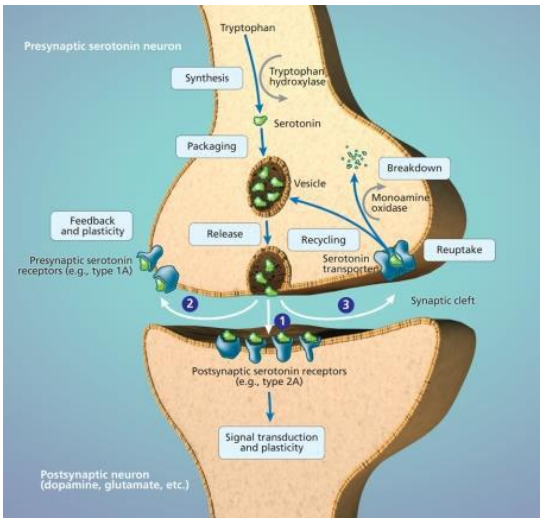

Figure 1: The serotonin synapse. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2630359/

- Serotonin is synthesized from tryptophan by tryptophan hydroxylase and packaged in vesicles
- It then gets released into the synaptic cleft where it can activate the **post-synaptic serotonin receptors (type 2A)** and this result in the activation of signal transduction and induces plasticity
- Or it can bind to **presynaptic serotonin receptors (type 1A)** for feedback mechanisms and plasticity
- The last possible fate of serotonin in the synaptic cleft is to bind to the **serotonin transporter** to re-enter the presynaptic terminal (**reuptake**)
- Once serotonin has been taken inside the presynaptic terminal it can either be recycled or broken down by **monoamine oxidase**

The bolded items are the main targets of currently available antidepressants and it is easy to understand how all currently available antidepressants will somehow increase serotonin concentration in the synaptic cleft. However, there are other types of antidepressants that are concerned with norepinephrine and dopamine modulation as these two neurotransmitters' systems are also found to be dysfunctional in depressed patients.

- **Monoamine oxidase inhibitors** inhibit the breakdown of serotonin → increased recycling → increased serotonin concentration in the synaptic cleft
- **Tricyclic antidepressants** are non-selective serotonin and norepinephrine reuptake inhibitors
- **Selective serotonin reuptake inhibitors**, as the name implies, prevent the reuptake of serotonin by the serotonin transporter
- **Specific serotonergic antidepressants**

The Direct Effects of Antidepressants:

- Inhibition of serotonin, norepinephrine or dopamine transporters
- Monoamine oxidase inhibition
- Activation of serotonin type 1A receptors or sigma receptors

The Early Effects of Antidepressants:

- Increase the availability of serotonin, norepinephrine and dopamine in the synaptic cleft
- Increase the activation of monoamine neurotransmitter receptors
- The activation of adenylate cyclase and other intracellular signaling pathways
- Increased expression of neurotrophic factors (patients with major depressive disorder also have atrophy of certain brain regions → activation of neurotrophic factors is therefore helpful on the long-term)

The Long-term Effects of Antidepressants:

- Receptor adaptation → decreased efficacy and development of tolerance
- Increased plasticity and the formation of new synapses → long-term effects even after the discontinuation of the drug
- Antiapoptotic and neurogenesis effects → less brain atrophy
- Anti-inflammatory effects
- Decreased production of stress hormones such as cortisol and local neurotoxic effects related to cellular stress → improved cellular survival

References:

- First-Aid 2018

Selective Serotonin Reuptake Inhibitors:

Outline:

- Overview
- Mechanism of Action
- Clinical Uses
- Side Effects
- Serotonin Syndrome
- References

Overview:

- Selective serotonin reuptake inhibitors are the second-generation of antidepressants (after monoamine oxidase inhibitors and tricyclic antidepressants)
- They include fluoxetine, fluvoxamine, paroxetine, sertraline, escitalopram, and citalopram
- They have been used in clinical practice since 1987
- They are not safer than tricyclic antidepressants, they simply have a different side-effect profile
- Efficacy in major depressive disorder is from 22 to 48%

Mechanism of Action:

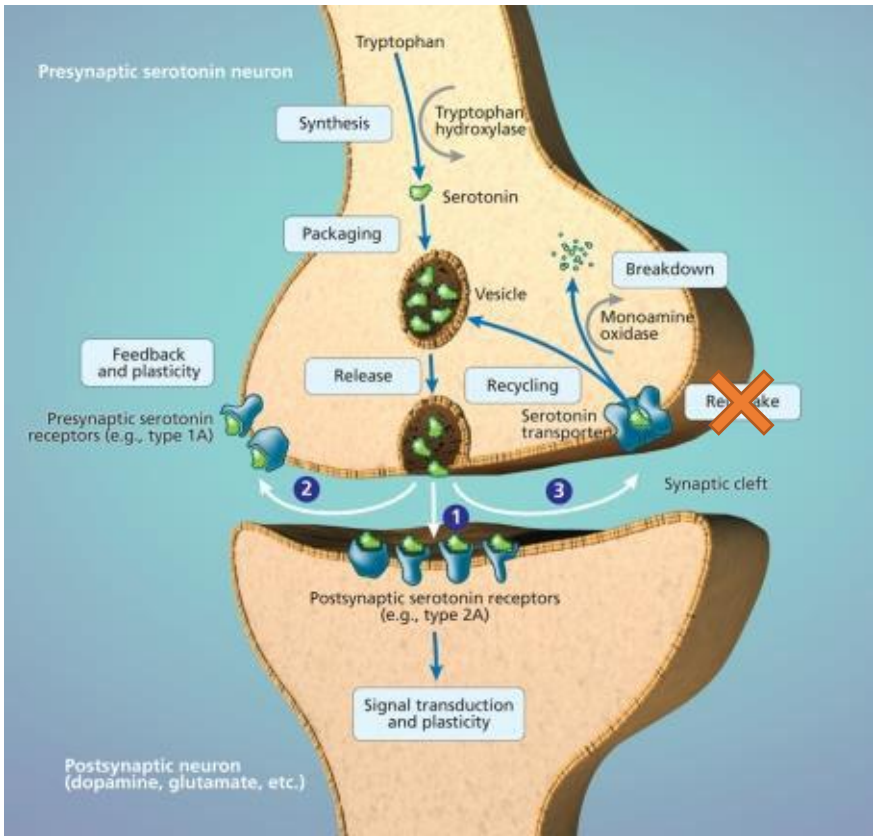

Figure 1: The serotonin synapse. SSRIs block serotonin transporter in the presynaptic membrane which increases the availability of serotonin in the synaptic cleft. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2630359/

- **Selective serotonin reuptake inhibitors**, as the name implies, prevent the reuptake of serotonin by the serotonin transporter

Clinical Uses:

- Major depressive disorder
- Generalized anxiety disorder
- Panic disorder
- Bulimia nervosa for bulimic symptoms
- Anorexia nervosa for comorbid depression and anxiety
- Obsessive-compulsive disorder
- Premenstrual dysphoric disorder
- Premature ejaculation
- Social anxiety disorder
- Post-traumatic stress disorder

Side Effects:

- Gastrointestinal distress
- SIADH
- Sexual dysfunction in the forms of anorgasmia and decreased libido

Serotonin Syndrome:

Causes and mechanism:

- Any drug that increases serotonin concentration in the synaptic cleft such as SSRIs, SNRIs, TCAs, or MAO inhibitors
- Can be also caused by tramadol, ondansetron, triptans, linezolid, dextromethorphan, and St. John's wort

Clinical features:

- **Increased neuromuscular activity**: clonus, hyperreflexia, hypertonia or seizures
- **Autonomic stimulation**: hyperthermia, diaphoresis, or diarrhea
- Agitation
- A psychiatric emergency
- Treated with cyproheptadine which is a serotonin type 2A receptor (post-synaptic) antagonist

References:

- First-Aid 2018

Serotonin Norepinephrine Reuptake Inhibitors:

Outline:

- Overview
- Mechanism of Action
- Clinical Uses
- Side Effects
- References

Overview:

- Evidence shows that the pathogenesis of depression involves serotonin and norepinephrine dysfunction
- This led to the development of dual acting antidepressants which in theory should be superior to single acting antidepressants
- Moreover, because they work on two different neurotransmitters, their applications are wider than SSRIs
- They include venlafaxine, desvenlafaxine, and duloxetine

Mechanism of Action:

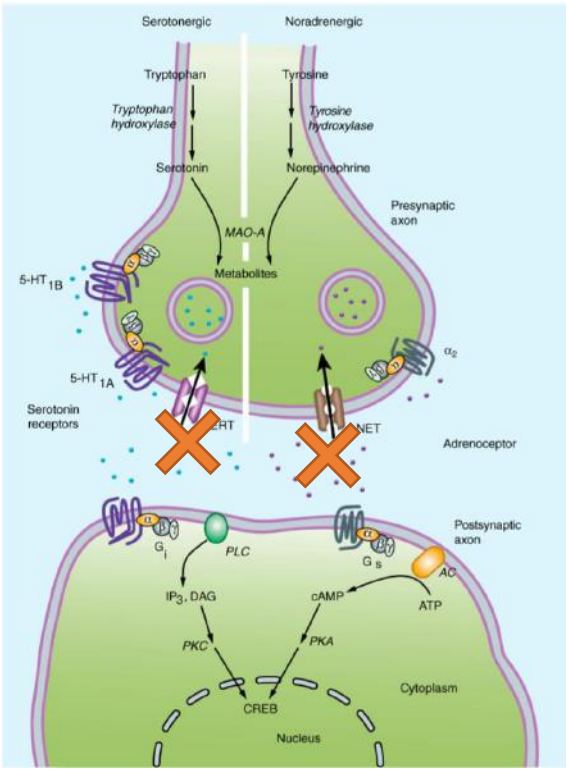

Figure 1: SNRIs bock norepinephrine and serotonin transporters, which inhibits norepinephrine and serotonin reuptake. Source: http://cdn.intechopen.com/pdfs/37606/InTech-Serotonin_noradrenaline_reuptake_inhibitors_snris_.pdf

- **Serotonin norepinephrine reuptake inhibitors**, as the name implies, prevent the reuptake of serotonin and norepinephrine by the serotonin and norepinephrine transporters → increase the synaptic concentration of serotonin and norepinephrine

Clinical Uses:

Venlafaxine:

- Depression
- General anxiety disorder, social phobia, panic disorder and vasomotor symptoms

Desvenlafaxine:

- Major depressive disorder and vasomotor symptoms of menopause
- Promising results in fibromyalgia

Duloxetine:

- Depression and anxiety disorders
- Stress urinary incontinence
- Diabetic neuropathy
- Fibromyalgia

Side Effects:

- Increase blood pressure → because of norepinephrine
- Stimulant effects
- Sedation
- Nausea

References:

- First-Aid 2018

Tricyclic Antidepressants:

Outline:

- Overview
- Mechanism of Action
- Clinical Uses
- Side Effects
- Toxicity
- Withdrawal
- References

Overview:

- Were discovered in the 1950s
- Contain three rings of atoms “tricyclic”
- They are considered as first-generation “not first-line” antidepressants
- Safety profile is similar to SSRIs, but their efficacy is inferior in the treatment of depression
- They include amitriptyline, nortriptyline, imipramine, desipramine, clomipramine, amoxapine and doxepin

Mechanism of Action:

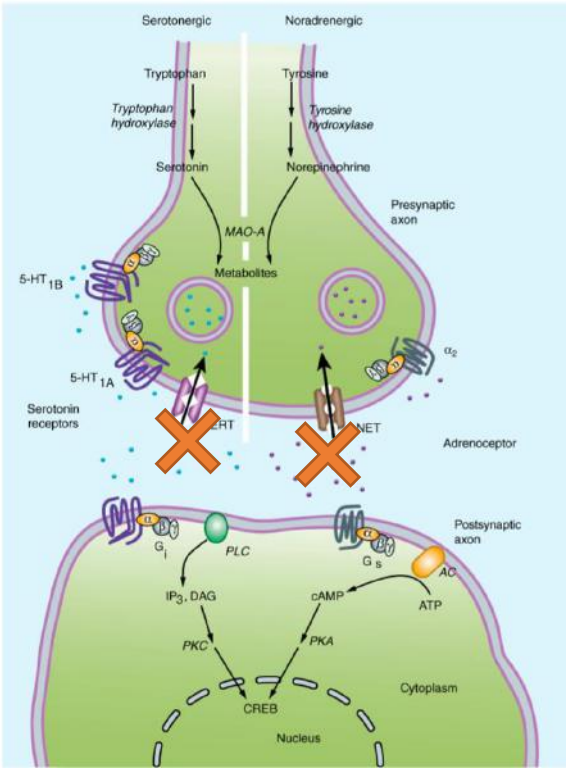

Figure 1: TCAs bock norepinephrine and serotonin transporters, which inhibits norepinephrine and serotonin reuptake. Source: http://cdn.intechopen.com/pdfs/37606/InTech-Serotonin_noradrenaline_reuptake_inhibitors_snris_.pdf

- **Tricyclic antidepressants** block norepinephrine and serotonin transporters → increase the synaptic concentration of serotonin and norepinephrine

Clinical Uses:

- Major depressive disorder, peripheral neuropathy, chronic pain, and migraine prophylaxis
- Nocturnal enuresis might respond to imipramine
- Clomipramine has some efficacy in obsessive-compulsive disorder

Side Effects:

Antimuscarinic-mediated side effects:

- Dry mouth
- Dry nose
- Blurry vision
- Constipation
- Urinary retention
- Cognitive and memory impairment
- Tachycardia

Other side effects:

- Sedation
- Alpha-1 effects such as postural hypotension
- Amitriptyline has more anticholinergic effects than nortriptyline
- QT interval prolongation

Toxicity:

- Convulsions
- Coma
- Cardiotoxicity due to Na channel inhibition
- Respiratory depression
- Hyperpyrexia
- Confusion
- Hallucinations
- Treat with $NaHCO_3$ to prevent arrhythmia

Withdrawal:

- Anxiety
- Insomnia
- Headache
- Nausea
- Malaise
- Motor disturbances

References:

- First-Aid 2018

Monoamine Oxidase Inhibitors:

Outline:

- Overview
- Mechanism of Action
- Clinical Uses
- Side Effects
- Hypertensive Crisis
- References

Overview:

- Monoamine oxidase inhibitors are first-generation anti-depressants
- They include tranylcypromine, phenelzine, and isocarboxazid
- Selegiline is a selective MAO-B inhibitor
- MAO is responsible for the breakdown of the principle monoamine neurotransmitters norepinephrine, serotonin and dopamine

Mechanism of Action:

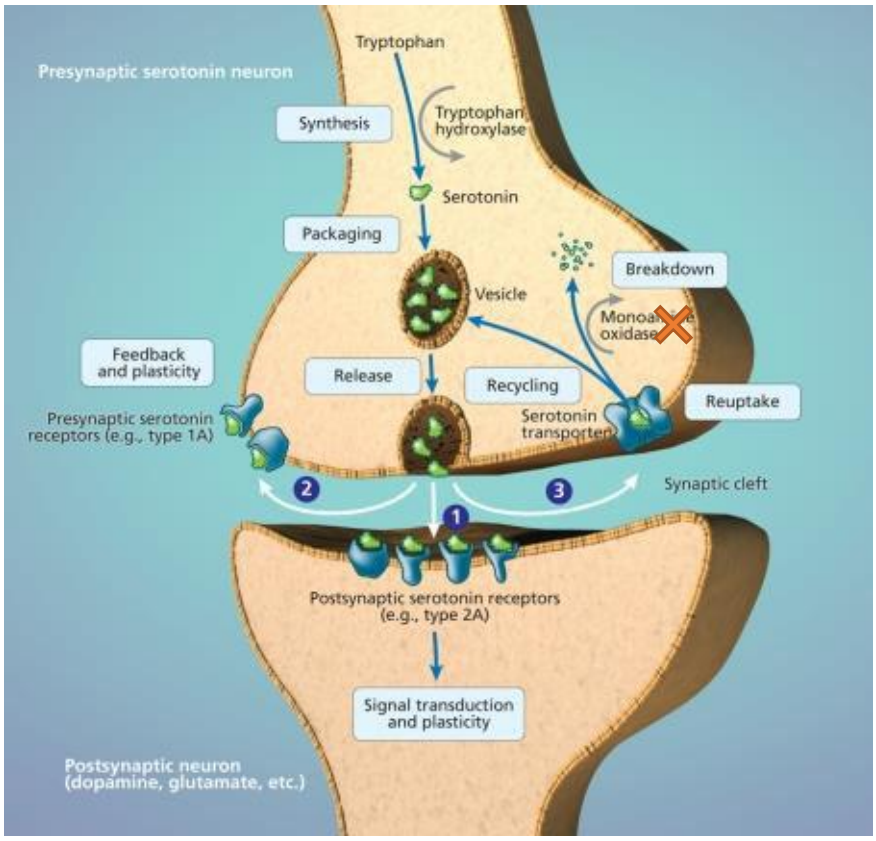

Figure 1: The serotonin synapse. MAO inhibitors inhibit monoamine oxidase which increases the amount of monoamine neurotransmitters available for recycling. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2630359/

- **Monoamine oxidase inhibitors**, as the name implies, inhibit the enzyme monoamine oxidase which is responsible for the breakdown of monoamine neurotransmitters

- Inhibiting this enzyme results in an increased concentration of norepinephrine, serotonin and dopamine in the synaptic cleft

Clinical Uses:

- Atypical depression
- Anxiety
- Parkinson disease (selegiline increases the concentration of dopamine in the synaptic cleft)

Side Effects:

- Contraindicated with SSRIs, TCAs, St John's wort, meperidine and dextromethorphan → can precipitate in serotonin syndrome
- If MAO inhibitors are discontinued, wait for at least two weeks before starting serotonergic drugs

Hypertensive Crisis

Causes and mechanism:

- Consuming tyramine-rich foods while taking MAO inhibitors
- Tyramine-rich foods include aged cheeses, wine and cured meats
- Tyramine displaces norepinephrine in the synaptic cleft → increased sympathetic stimulation

Clinical features:

- Hypertensive crisis

Treatment:

- Phentolamine

References:

- First-Aid 2018

Atypical Antidepressants:

Outline:

Overview:

- The typical antidepressants (MAO inhibitors, SSRIs, SNRIs, and TCAs) can cause unfavorable side effects that could adversely affect their tolerability
- This led to the development of atypical antidepressants which do not fit neatly in any class of the typical antidepressants
- The atypical antidepressants have a favorable side-effect profile

Bupropion:

Mechanism of action:

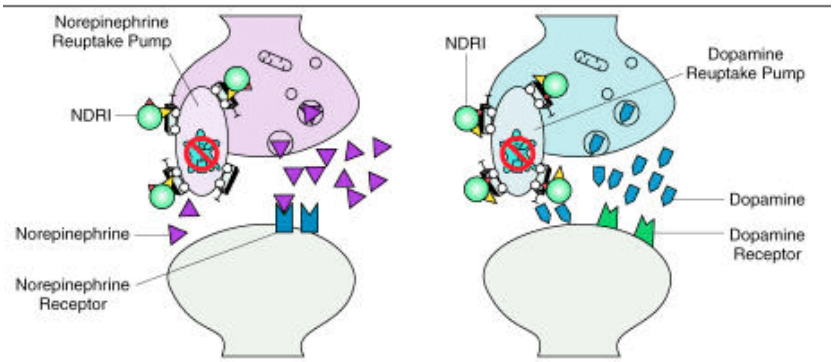

Figure 1: Mechanism of action of bupropion, a norepinephrine-dopamine reuptake inhibitor (NDRI). Source: https://www.restartmed.com/wp-content/uploads/2017/09/mechanism-of-action-of-wellbutrin-for-weight-loss.png

- Bupropion is a norepinephrine-dopamine reuptake inhibitor that inhibit both transporters → increasing the concentration of norepinephrine and dopamine in the synaptic cleft

Clinical uses:

- Depression
- Smoking cessation

Side effects and toxicity:

- It can cause tachycardia and insomnia → because of excess norepinephrine
- It might result in headaches
- Seizures in anorexia nervosa and bulimic patients

- Less likely to result in sexual side effects when compared to typical antidepressants

Mirtazapine:

Mechanism of action:

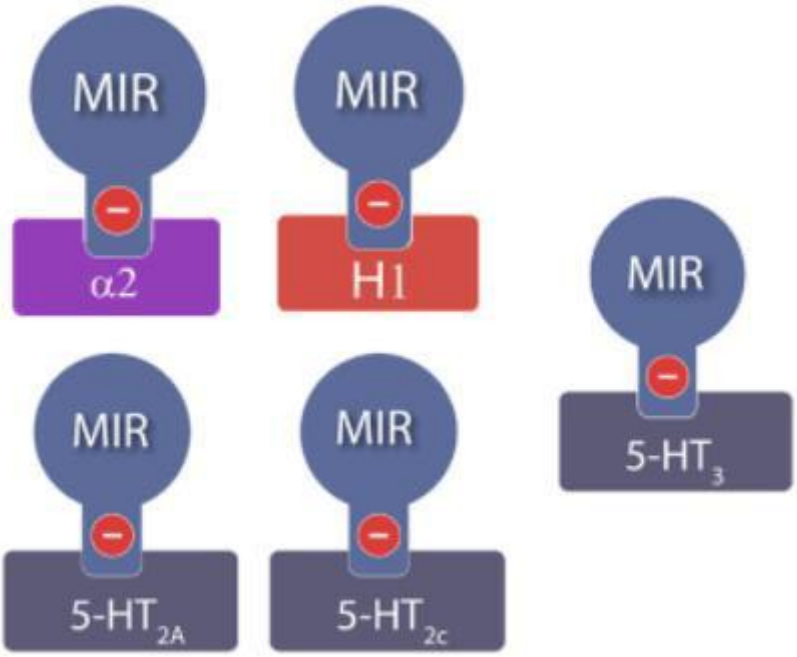

Figure 2: Mirtazapine blocks alpha-2, H1, serotonin 2A, 2C and type 3 receptors. Source: https://psychopharmacologyinstitute.com/antidepressants/mirtazapine-essentials-every-prescriber-know/

- The blockade of alpha-2 receptors increases the release of norepinephrine and serotonin

Clinical uses:

- Major depressive disorder
- Depression patients with insomnia
- Increase food intake → desirable in anorexic patient

Side effects and toxicity:

- Sedation due to H1 receptor blockade
- Weight gain
- Dry mouth

Trazadone:

Mechanism of action:

- Inhibits serotonin type2, alpha-1-adrenergic and H1 receptors

Clinical uses:

- Treatment of insomnia

Side effects and toxicity:

- Sedation
- Nausea
- Priapism
- Postural hypotension

Varenicline:

Mechanism of action:

- Partial agonist of nicotinic Ach receptors
- Prevents nicotine from binding to its receptors “competitive with nicotine”

Clinical uses:

- Smoking cessation

Side effects:

- Sleep disturbances
- Depression

Vilazodone:

Mechanism of action:

- Inhibits serotonin reuptake → increasing serotonin concentration in the synaptic cleft
- Serotonin type 1A receptor partial agonist

Clinical uses:

- Major depressive disorder

Side effects and toxicity:

- Headache
- Diarrhea and nausea
- Weight gain
- Dry mouth
- Tachycardia
- Should be used cautiously with other serotonergic agents due to high risk of serotonin syndrome

Vortioxetine:

Mechanism of action:

- Inhibits serotonin reuptake. Also, a serotonin receptor type 1A agonist and type 3 antagonist

Clinical uses:

- Major depressive disorder

Side effects and toxicity:

- Nausea
- Sexual dysfunction

- Sleep disturbances in the form of abnormal dreams
- Anticholinergic effects
- Increased risk of serotonin syndrome if taken with other serotonergic agents

References:

- First-Aid 2018