Chapter 5

Anxiety-related Disorders

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Abstract

Anxiety is a common experience, a physiologic mechanism that lets us cope with a stressor, but if it occurs without a stimulus or it is exaggerated and general functioning is impaired, it becomes pathological. Treating anxiety disorders requires pharmacotherapy to lower anxiety levels and psychological therapies to learn to cope with stressors adaptively.
Obsessive-Compulsive Disorder (OCD) has been considered as part of the Anxiety Disorders chapter up to the fourth edition of the DSM (DSM IV-TR), while from the fifth edition (DSM- 5) it is placed in a separate chapter. The nosographic autonomy of this disorder depends on the fact that the anxious manifestations, even if present, would be secondary and dependent on the obsessive contents. A group of conditions related to OCD from a clinical, epidemiological and sometimes etiopathological perspective is included in the DSM chapter about "Obsessive-compulsive and related disorders".
After a traumatic experience, one person physiologically develops a limited-in-time reaction. In some cases, more pronounced depressive, anxious, intrusive and/or dissociative symptoms occur. The biological basis for trauma-related disorders is not fully understood, but insights so far have let us choose pharmacological treatments alongside with psychotherapy in order to control symptoms and elaborate the traumatic experience

Keywords: Anxiety; Avoidance; Stress; Trauma; OCD; Obsession; Compulsion.

5.1 ANXIETY DISORDERS

5.1.1 DEFINITION

Commonly speaking, anxiety is perceived as a negative feeling or an obstacle to the person's overall functioning. In origin, anxiety is an innate process of the organism, selected by evolution and present in all animals, whose function is to trigger reactive and adaptive responses aimed at survival and self-preservation.

The concept of physiological anxiety comes close to the concept of fear that we have in common with other animals and is the emotional response to an imminent threat, while anxiety is a typically human emotion, connected to the sense of time, which refers to the anticipation of a future threat that is not always precisely identifiable. The two states can of course coexist but they differ because while the first is more oriented to a defence reaction through the fight or flight, that is to move away from danger (attack/flight reaction), anxiety has the function of predisposing the subject to a behavioural response. The imminent, perceived or real danger, through a state of vigilance or alert that leads to prudent or avoidance behaviour.

We therefore speak of "physiological anxiety" for a state of psychic alert in which, in front of a stimulus perceived as threatening or dangerous, the organism puts in place a series of mechanisms aimed at improving performance and an adaptive response to the threat. This alarm reaction allows the organism to recruit all the resources to defend its integrity. The result is an increase of vigilance, attention and ability to react against a perceived danger.

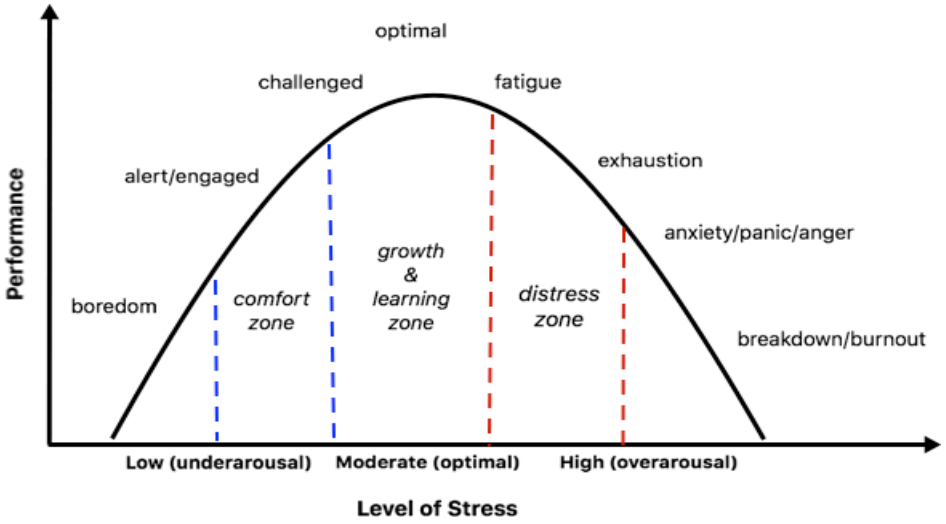
This process is innate and shared by all individuals, although it varies in its expression and intensity based on the subjective component - that is the personal background and experience - and determines how a given stimulus is perceived. From this also derives the importance of environmental factors and life events in determining the threshold for activation of the alert state and, therefore, the extent of the anxious response. In addition to inter-individual differences, there can also be intra-individual differences: the anxious reaction to a given circumstance can vary throughout the life of a subject based on previous experiences, outcomes and feedback. Physiological anxiety should therefore be considered advantageous, as it is functional and adaptive to the integrity of the individual.

On the contrary, "pathological anxiety" occurs when the reaction to an anxiogenic stimulus is dysfunctional or disadvantageous, for example it compromises the individual's ability to react, up to a condition of inhibition on a behavioural and mental level which can result in clumsy movement and loss of lucidity, instead of an adequate psychophysical reaction, resulting therefore in maladaptive behaviour.
Anxiety can also be defined as "pathological" in relation to the stimulus: a person can have an anxious reaction in the absence of a real stimulus or an anxious reaction that is disproportionately excessive or prolonged for the stimulus itself.
In psychiatry, the term "anxiety" refers to a pathological condition that is connoted as an emotional state with a markedly unpleasant content and associated with a condition of disproportionate alarm: it is characterized by a sense of apprehension, uncertainty, fear and alertness, with anticipation of negative events towards which the person feels hopeless and helpless. It is often linked to hypothetical dangers, which are anticipated at the level of thought and feelings, imagined, and projected into the future. In pathological anxiety, the subjective component is more important than the extent of the dangerous event itself.
Characteristics of anxiety are that it is anachronistic (erroneous anticipation of the damage: a threat is expected in the future but it is perceived as already present now and catastrophically), phantasmatic (representation of imagined dangers that are not really present) and stereotyped (it is often repetitive because it is linked to the patient's cognitive distortion).

Lastly, anguish is an anxious mood state of even greater intensity, with a marked sense of oppression, restlessness and the perception of despair and even physical pain or tightness.

The figure shown here represents the Yerkers-Dodson curve, which relates the intensity of anxiety with the efficiency of the performance: it allows depicting the continuum that exists between physiological (adaptive) and pathological (maladaptive) anxiety. A normal degree of anxiety is required for a satisfactory performance: in the first phase, as the level of anxiety increases, the

individual's performance improves up to an optimal level. If the level of anxiety continues to increase, the physical and cognitive performances decrease and become dysfunctional up to a total inability to react.



By the term “adaptive anxiety”, we indicate those anxiety reactions that lead to the improvement of performance; planning and adaptation to the environment and that require an adequate level of vigilance. The optimal level of the Yerkes-Dodson curve is that corresponding to a state of activation in which psychic and somatic systems prepare the individual for the most appropriate reaction for that specific situation - that can be altogether referred to the “flight or fight” response.
An important characteristic of adaptive anxiety concerns its duration, which must be limited in time and end with the suspension of the stimulus.
If the level of anxiety continues for prolonged times, this results in a consumption of resources until they are totally exhausted and one would slip into a state of maladaptive anxiety.
“Maladaptive anxiety” is a reaction that is disproportionate in terms of intensity and/or duration with respect to the inducing stimulus. This involves a progressive consumption of resources, which is followed by a decrease in performance, as shown in the right part of the Yerkers-Dodson curve. Anxiety is maladaptive even when the alarm state is activated in response to a stimulus that is not actually dangerous or in the absence of stimulus at all.

5.1.2 ETIOPATHOGENESIS

Physiological mechanisms of stress response

A sensory system (e.g. sight, hearing) perceives the danger and transmits the message through the ascending reticular formation to the thalamus and the limbic system. The thalamus stimulates the hypothalamus and activates the endocrine system and the sympathetic nervous system, initiating the body's response to stress. The thalamus performs a primary relais function between the exteroceptive sensory systems and the primary sensory areas of the cerebral cortex, which then project to the associative areas for an integrated processing of the stimulus. From the cortex, the information is then transferred to subcortical structures involved in affective, behavioural and somatic responses. The main of these subcortical areas is the amygdala, a subcortical nucleus responsible for the acquisition and expression of conditioned fear, with a wide spectrum of reciprocal connections with the cortical and limbic structures involved in the multisystemic response to stress. From these cortical and subcortical areas, signals are sent to the brainstem and hypothalamus, resulting in the autonomic, endocrine and behavioural response of fear.

The anxious response consists of a cascade of finely tuned physiological processes that result in various modifications aimed to cope with the threatening stimulus. Three phases can be distinguished:

- *First phase*: alarm. The phase of shock, of fright, when a threatening stimulus is presented, and during which energy resources are mobilized through biochemical and hormonal responses. It has a latency of a few seconds and prepares the body to deal with the dangerous situation. The organism perceives, consciously or unconsciously, a stress factor (physical, psychological or biological), that is something unexpected, new or unusual, able to represent a difficulty or a potential danger and therefore implements a cascade of lightning-fast responses to try to survive the threat. Whatever the cause, the biochemical process of the stress reaction is the same. The hypothalamus, which, in addition to other brain areas, is closely connected with the endocrine and immune system, causes numerous chemical and electrical changes in the body. In particular, this activation causes the secretion of specific hormones such as cortisol and, through a direct brain-adrenal gland connection of the orthosympathetic nervous system, adrenaline and noradrenaline, which will recruit various organs important for the response; production of beta-endorphins, the body's own innate painkillers that raise the pain threshold. The effect is an increase in metabolism. Blood from peripheral areas (peripheral vasoconstriction and coagulation facilitation, important in case of wounds) and secondary organs are directed to the most necessary ones (heart with increased range, lungs with tachypnea, muscles whose tone increases) to maximize efficiency. The skin becomes pale, sweaty and cold. Digestive function tends to stop, causing nausea. Blood circulation also decreases in areas of the brain that specialize in processing information and solving problems: therefore, anxiety increases and concentration decreases.
- *Second phase*: resistance or adaptation. The duration of each stress reaction depends above all on this phase, which lasts as long as special promptness and capacity for action is required. It is the phase in which one adapts to the new circumstances, the body reacts to the threatening stimulus by using its resources to cope with the danger as long as it persists. In this phase, the hypothalamus-pituitary-adrenal axis plays a fundamental role. The fundamental event is the overproduction of cortisol, which results in the down-regulation of the immune system (reduction in the absolute number of NK cells, alteration of the CD4/CD8 ratio, increase in circulating neutrophils, reduced proliferation of lymphocytes and phagocytosis of neutrophils). There is an increase in the expression of IL-1, IL-6, TNF-α, reduction of IL-2, INF-γ and MHC-II, reduced activity of NK cells): this is not worrying in the short term but becomes a problem in case of chronic stress.
- *Third stage*: exhaustion. Once the anxious stimulus stops, the physiological mechanisms gradually die out. It is fundamental as a prolonged stressful condition creates the situation of pathological maladaptive anxiety, which is associated with the consumption of energy resources (catabolic state) of the body. It starts in a few minutes and can last a long time. When the danger is overcome or when the energy is totally consumed, the final phase of the stress response begins, which aims to ensure the body the necessary rest period. The exhaustion phase is felt like a significant drop in energy associated with relief or pleasant numbness. Biochemically, the exhaustion phase begins with a rapid decrease in adrenal hormones (adrenaline, noradrenaline, and cortisol) and energy reserves. The parasympathetic system takes over the control of the vegetative system: normal blood flow in the digestive system, brain and skin is restored.

Neuroimaging studies have shown that anxiety disorders have been related to both hyperactivity of the amygdala and decreased activity of the hippocampus, a condition that leads to excessive activation of the hypothalamus-pituitary-adrenal system (HPA).

Chemical basis of anxiety

The neurotransmitters mainly involved in anxiety disorders are serotonin and noradrenaline, in particular studies have demonstrated:

- An increase in serotonin turnover at the level of the prefrontal cortex, amygdala and lateral hippocampus;
- Central hyperactivity of noradrenaline, with downregulation of postsynaptic α-2 adrenergic receptors.

Norepinephrine dysregulation is associated with the onset of panic attacks, in Klein's theory of the "false suffocation alarm". Around the 90s, it was seen that inhaling CO2 in subjects predisposed to anxiety (increasing the partial pressure of CO2 as it occurs with tachypnea, a frequent phenomenon in anxious subjects) led to hyper-activation of respiratory chemoreceptors, with metabolic alkalosis, direct stimulation of the Locus Coeruleus and hypoxia. Subjects have hypersensitivity to these suffocation signals such that, following a false alarm signal, they develop a panic attack.
Other neurotransmitters involved are:

- GABA: the role of the GABAergic system is highlighted by the action of BDZ in anxiety. The system is widely distributed in the hippocampus, amygdala, frontal and occipital cortex.
- Dopamine (DA): subjects with high levels of trait anxiety, particularly predisposed to developing panic attacks, seem to show an increase in the central activity of the dopaminergic pathways (in particular, frontal cortex).
- Some neuropeptides also participate in the anxiety response, with collateral functions: Cholecystokinin (CCK), Corticotropin-releasing factor (CRR), Tachykinins as substance P, neurokinin A and B are abundantly expressed in the circuits connected to anxiety.

5.1.3 CLINICAL PRESENTATION

Anxiety Disorders are the most common mental disorders, with a prevalence greater than 28%; they often develop in adolescence or early adulthood and are twice as frequent in women. They can often be accompanied by depressive symptoms, particularly when the anxiety problem continues over time, and substance abuse/addiction (substances, medications and alcohol).
A characteristic of anxiety is the presence of fluctuating levels of intensity and duration. It has a tendency to pervasiveness, markedly conditioning the life of those affected. It is perceived as a threat to one's integrity that generates a condition of apprehension and expectation of damage, which is associated with the cognitive distortion of pejorative amplification of reality and, therefore, a feeling of helplessness and despair.
A symptom frequently encountered in patients is insomnia, with difficulty falling asleep and with a sleep fragmented by numerous awakenings.

As anticipated above, there are many systems and organs involved in the anxious response. Their involvement explains the somatic equivalents that accompany psychic anxiety and that are frequently found in Anxiety Disorders.

- Cardiovascular system
    1. Increased heart rate and output
    2. Increased blood volume and blood pressure
    3. Peripheral vasoconstriction

4. Coronary dilation
5. Positive cardiac inotropic effect
6. Increase in blood levels of glucose, free fatty acids, cholesterol

- Respiratory system
  1. Increased oxygen exchange
  2. Tachypnea
- Digestive system
  1. Xerostomia
  2. Contractions of the oesophagus
  3. Increase in gastric acid secretion
  4. Changes in peristalsis
- Metabolic effects of catecholamines
  1. Activation of glycogenolysis and lipolysis
  2. Increase in free fatty acids, glucose and lactate
- Muscles, skin, immune system
  1. Increased muscle tone
  2. Increased smooth muscle contractions
  3. Increased perspiration
  4. Decreased skin temperature
  5. Reduction of immune activity

5.1.4 TREATMENT

The therapeutic approach of Anxiety Disorders involves the integration of psycho-educational interventions, psychotherapeutic interventions and somatic therapy (mainly pharmacological).

- Psycho-educational interventions consist of explaining the mechanisms underlying the anxious response to the patient, e.g. it is normal to have a fast heartbeat, shallow breathing and tightness in the chest as the body prepares for an attack and flight reaction.
- Psychotherapy aims at a cognitive restructuring of the patient's way of facing the perceived dangerous situation; the most used are cognitive-behavioural therapy, desensitization with imaginative and in vivo exposure, autogenic training, social skills training, various relaxation techniques and biofeedback.
- Somatic pharmacological therapy is similar for all anxiety disorders and uses drugs with a purely symptomatic purpose, with a rapid but short-term effect and drugs with a delayed but long-term effect. Among the somatic non-pharmacological therapies, the most recent is Transcranial Magnetic Stimulation (TMS), which can be used as an enhancement of drug therapy.

Pharmacotherapy

The degree of discomfort of the patient is often very high and requires a pharmacological intervention that is often effective to reduce the intensity of anxiety while taking into account possible side effects. In addition to reducing anxiety levels, one of the first objectives to be achieved with drug therapy is the restoration of good sleep, often compromised in Anxiety Disorders.

The ideal is personalized therapy, which is a therapy tailored as much as possible to the patient's profile and needs. Before setting up a drug therapy, an accurate mental state examination is required, accompanied by a thorough medical history interview with particular attention to the psychopharmacological history. A careful medical history must also be conducted, concerning the presence of possible organic pathologies that may affect the choice of the drug. Another principle is

to give a therapy that is as simple as possible, with the least possible number of drugs at the minimum effective dosage.

The choice of the drug, with the expected results, the latency times to be able to observe the first benefits and their possible side effects must be shared with the patient. Sometimes, and only with the patient's permission, it may be appropriate to provide adequate information also to family members accompanying the patient to the visit regarding drug therapy, in order to optimize adherence to treatment by the patient who in such way feels supported by family members.

During the entire duration of the drug treatment, it is important to monitor the occurrence of possible or probable side effects and any interactions with other concomitant therapies, especially in elderly patients.

Pharmacological therapy used are:

- Antidepressants:
    - Selective Serotonin Reuptake Inhibitors (SSRIs)
    - Serotonin / Norepinephrine Reuptake Inhibitors (SNRIs)
    - Tricyclics antidepressants (TCAs)
    - Atypical antidepressants
- Benzodiazepines
- Beta-blockers
- Anticonvulsants

The class of drugs of first choice is that of antidepressants and in particular selective serotonin reuptake inhibitors (SSRIs). Benzodiazepines (or other symptomatic drugs such as beta-blockers and some antiepileptic drugs with anxiolytic action such as gabapentin and pregabalin) are often used in combination, at least in a first phase and for a limited time, especially when acute symptoms require rapid action (e.g. high levels of anxiety with its somatic correlates, panic attacks, insomnia). In any case, it will be appropriate to reduce their use, as soon as possible, since benzodiazepines give tolerance and dependence and have a consequent potential of abuse.

5.1.5 CLASSIFICATION

Anxiety disorders are clinical conditions characterized by pathological anxiety that can be distinguished from each other based on the type of objects or situations that determine it, which are associated with cognitive distortions and avoidance behaviours. Clinical evaluation to determine whether fear or anxiety is excessive or disproportionate must also take into account the patient's cultural context.

Anxiety disorders in the category of Anxiety Disorders according to DSM-5 are:

- GENERALIZED ANXIETY DISORDER
- PANIC DISORDER
- SPECIFIC PHOBIA
- SOCIAL PHOBIA
- SELECTIVE MUTISM
- SEPARATION ANXIETY
- ANXIETY INDUCED BY SUBSTANCES / DRUGS
- ANXIETY DUE TO ANOTHER MEDICAL CONDITION
- ANXIETY DISORDER WITH ANOTHER SPECIFICATION

- ANXIETY DISORDER WITHOUT ANY OTHER SPECIFICATION

5.1.5.1 GENERALIZED ANXIETY DISORDER (GAD)

General Anxiety Disorder (GAD) is characterized by a chronic state of apprehension, with concerns of a diffuse and multifocal nature. Patients present various physical symptoms (headache, lower back pain, gastrointestinal disorders) and they frequently seek internists and other speciality physicians in the belief that such symptoms are the expression of an organic problem. Only 33% of subjects with GAD point their distress back to a psychological origin from the very beginning and refer directly to a psychiatrist.

Epidemiology

This form of disorder is the most frequently encountered. In the United States, it has a prevalence of 5-11%, in Europe of 4.3-5.9%, with a double prevalence in females. It has a typical onset in late adolescence or early adulthood.

GAD generally has a chronic course but can have fluctuations in terms of intensity.

Comorbidities:

50-90% of patients have comorbidity with other disorders, in particular social phobia, specific phobia, panic attacks or even depression. It is common to find abusive behaviours that can be substances or drugs (anxiolytics).

Clinical Presentation

The patient has a pervasive state of frequent concern that persists and appears to be disproportionate to the extent of the threat over which the patient has no control.

The symptomatology of GAD is very varied and changeable:

- cognitive level: feeling nervous or on a tightrope, having exaggerated alarm responses, difficulty concentrating, light-headedness, inability to relax, difficulty falling asleep, irritability, apprehensive attitude, fear of being able to deal with situations
- somatic level: dyspnoea and a feeling of suffocation, palpitations, sweating or cold and wet hands, dry mouth, dizziness or a feeling of dizziness, nausea, diarrhoea or other abdominal discomforts, hot flushes, or chills, urinary discomfort, dysphagia or "knot in the throat ", tremors, muscle twitching, muscle tension or pain, easy fatigue.

DSM-5 diagnostic criteria:

A. “Excessive anxiety or worry" experienced most days over at least six month and which involve a plurality of concerns.

B. Inability to manage worry.

C. At least three of the following occur:

1. Restlessness
2. Fatigability
3. Problems concentrating
4. Irritability

5. Muscle tension
6. Difficulty with sleep

D. Note that in children, only one of the above items is required.

E. One experiences significant distress in functioning (e.g., work, school, social life).

F. Symptoms are not due to drug abuse, prescription medication or other medical condition(s).

G. Symptoms do not fit better with another psychiatric condition such as panic disorder.

Differential diagnosis

It must always be borne in mind that a clinical picture with anxiety symptoms and physical symptoms may in the first place depend on an underlying organic pathology, which must, therefore, always be considered. In particular, the following organic and other psychiatric pathologies must be considered in the differential diagnosis:

- Hyperthyroidism
- Paroxysmal supraventricular tachycardia
- Pheochromocytoma
- Hypoglycaemic crisis
- Complex partial seizure
- Mitral prolapse
- Respiratory pathologies
- Dizzy syndromes
- Anxiety disorder due to another medical condition
- Induced anxiety disorder
- Depression
- Phobias
- Conversion disorder

Treatment

GAD therapy includes antidepressants, in particular SSRIs as drugs of first choice. Antidepressant therapy generally lasts 6-12 months; however, there is often the need to continue treatment in the long term given that GAD is chronic in nature. There is a relapse in 25% of patients 1 month after stopping treatment and in 60-80% within one year after stopping drug therapy.

For symptomatic purposes, especially in the early periods of treatment, it may be necessary to combine therapy with anxiolytics such as benzodiazepines. Mid-life benzodiazepines are preferred, e.g. delorazepam, in divided doses (usually twice a day) to limit both the side effects of long half-life benzodiazepines (somnolence) and the plasma peak effect (which produces rapid but transient effect).

5.1.5.2 PANIC DISORDER

A panic attack is a massive and acute crisis that arises quickly and lasts a few minutes. It is an episode of intense alertness, anguish, fear or discomfort during which a variable number of physical and cognitive symptoms can occur suddenly and reach a peak within a few minutes. Panic attacks can be unexpected when they appear suddenly and for no apparent reason, even at night thus awakening the patient, or situational, when they occur in correlation to situations that the patient particularly fears and in which he experiences growing fear of being sick until the end of the panic attack. About half of patients have both types of panic attacks. Situational or expected ones are characterized by the presence of anticipatory anxiety concerning being able to find oneself in a certain situation or place: anticipatory anxiety is the "fear of fear", a state in which negativity, fear and worries related to a

specific event are anticipated with the thought and the person already experiences them as if it were present at the moment.
A single panic attack is not enough to make a diagnosis of panic disorder. Panic Attack Disorder (PAD) is when panic attack episodes recur over time, causing fear of following panic attacks and interference with normal functioning.

Epidemiology
10-15% of the general population experiences an unexpected panic attack at some point in their life. Of these, 3-4% develop a PAD with clinical relevance.
PAD has a prevalence of 1-4% in the general population, with the ratio F: M = 3: 1. The typical onset is in young adulthood (20-30 years).
The symptoms are varied and are neurological (44%), cardiac (39%) and gastrointestinal (33%). The trend of symptoms is varied as well as the frequency of attacks, which can be daily or interspersed with weeks or months. The trend is therefore fluctuating with phases of remission alternating with phases of recrudescence in periods of particular stress.

Pathogenic hypotheses
- Genetic predisposition: a higher prevalence of PAD is observed in first degree relatives (7-21%) compared to the general population; concordance between monozygotic twins (22-73%) is greater than that between dizygotic twins (0-11%);
- Respiratory hypothesis: Klein's false alarm theory of suffocation (noradrenergic and locus coeruleus hyperactivity in response to false hypoxia alarm, which determines the sensation of suffocation);
- Dysregulation of the brainstem and the cardiac-respiratory-vestibular system.

Clinical presentation
Criterion B in DSM-5 (at least one of the attacks is followed by a period of at least one month of persistent concern about the consequences of the attacks (loss of control, heart attack, fear of going crazy) and behavioural changes (need for companionship in certain situations, avoidance, for example for embarrassment or fear of being negatively judged by others precisely because of the symptoms of panic evident on the outside) illustrates the two key factors of the so-called panic loop. The panic loop is the conditioning process of the person concerning the association of situations/events as triggers the panic attack: by associating a certain situation with the panic attack, the patient begins to feel discomfort and fear for that situation and will decide to avoid it, or he will change his lifestyle and habits, for fear of having another panic attack.

<u>DSM-5 diagnostic criteria:</u>

A. Recurrent unexpected panic attacks. A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur;

Note: The abrupt surge can occur from a calm state or an anxious state.
1. Palpitations, pounding heart, or accelerated heart rate.
2. Sweating.
3. Trembling or shaking.
4. Sensations of shortness of breath or smothering.
5. Feelings of choking.

6. Chest pain or discomfort.
7. Nausea or abdominal distress.
8. Feeling dizzy, unsteady, light-headed, or faint.
9. Chills or heat sensations.
10. Paraesthesia (numbness or tingling sensations).
11. Derealisation (feelings of unreality) or depersonalization (being detached from oneself).
12. Fear of losing control or "going crazy."
13. Fear of dying.

Note: Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen. Such symptoms should not count as one of the four required symptoms.

B. At least one of the attacks has been followed by 1 month (or more) of one or both of the following:

   1. Persistent concern or worry about additional panic attacks or their consequences (e.g., losing control, having a heart attack, "going crazy").

   2. A significant maladaptive change in behaviour related to the attacks (e.g., behaviours designed to avoid having panic attacks, such as avoidance of exercise or unfamiliar situations).

C. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism, cardiopulmonary disorders).
D. The disturbance is not better explained by another mental disorder (e.g., the panic attacks do not occur only in response to feared social situations, as in social anxiety disorder: in response to circumscribed phobic objects or situations, as in specific phobia: in response to obsessions, as in obsessive-compulsive disorder: in response to reminders of traumatic events, as in posttraumatic stress disorder: or in response to separation from attachment figures, as in separation anxiety disorder).

We speak of a complete panic attack when at least 4 of a list of 13 symptoms are present. Sometimes the symptoms reported are fewer and in the case of a paucisymptomatic panic attack.

<u>Complications of the panic loop are:</u>

- Agoraphobia: development of avoidance behaviours for places or situations from which it would then be difficult to move away or in which they may not receive help in the event of a panic attack. In these cases the patient tends to identify the phobic partner in a family member or a person of reference, that is, the one who must be present to face the feared situations and who, being aware of his problem, can intervene and provide assistance if necessary, resulting in a significant limitation of the patient's autonomy and freedom of movement. Up to 50% of individuals with PAD develop agoraphobia;
- Abuse of substances with an anxiolytic effect (alcohol, benzodiazepines, cannabinoids): they are used as self-medication for anticipatory anxiety;
- Hypochondria: patients with panic attacks often go repeatedly to the emergency room fearing they have a serious physical illness;
- Secondary depressive syndrome.

Differential diagnosis:

- Hyper/hypothyroidism
- Hypoglycaemic crisis
- Pheochromocytoma
- Heart attack or angina
- Alterations of perception: déja vu, déja vecu, hallucinations.
- Asthmatic attack
- Abuse of stimulants (caffeine, amphetamines, cocaine)
- Alcohol and benzodiazepine withdrawal.
- Temporal lobe epilepsy

Treatment

Treatment is mainly based on antidepressants, of which the first choice falls on paroxetine. Therapy should be prolonged for at least 6-12 months before going to evaluate a possible reduction of drugs, after which the maintenance dosage is half the attack dose. In the case of panic disorder, there may be a resolution of the disorder, so once the patient is cured and is stable, they may no longer have panic attacks in the course of their life. This happens in 35-50% of patients, with improved response rates particularly seen in patients with agoraphobia. However, the therapy is ineffective in 20-30% of cases.

In case of acute panic attack or in the case of anticipatory anxiety, benzodiazepines with a short half-life can be prescribed for symptomatic purposes, e.g. alprazolam 0.5-1 mg. Who assists the patient during a panic attack can reassure them, stimulate a diaphragmatic breathing that allows better oxygenation of the blood, and provide a paper bag to help them in ventilation.

5.1.5.3 AGORAPHOBIA

Clinical definition and presentation

It is the anxiety related to being in embarrassing places or situations or from which it would be difficult to get away or in which help may not be available in the event of a panic attack.

Characteristic agoraphobic triggers are crowded or closed places (stadiums, shopping malls, cinemas, means of transport queuing in traffic, tunnels), wide-open spaces (freeways, bridges, wide streets, squares). These situations are avoided, reduced or endured with much discomfort and with the constant anxiety of having a panic attack, severely limit the patient's autonomy and quality of life.

Epidemiology

Agoraphobia is mostly found in association with a clinical history of panic attacks (with a prevalence of 1.1%); however, the presence of agoraphobia alone without panic attacks is possible (prevalence of 0.8%). It has a chronic course and a prevalence of 2-6% in the general population.

Comorbidities:

Agoraphobia can also be associated with other anxiety disorders (49-64%) and depressive disorders (33-52%). In one-third of cases, there is concomitant substance abuse.

DSM-5 diagnostic criteria:

A. Marked fear or anxiety about two (or more) of the following five situations:
   1. Using public transportation (e.g., automobiles, buses, trains, ships, planes).
   2. Being in open spaces (e.g., parking lots, marketplaces, bridges).

3. Being in enclosed places (e.g., shops, theatres, cinemas).
4. Standing in line or being in a crowd.
5. Being outside of the home alone.

A. The individual fears or avoids these situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symptoms or other incapacitating or embarrassing symptoms (e.g., fear of falling in the elderly; fear of incontinence).
B. The agoraphobic situations almost always provoke fear or anxiety.
C. The agoraphobic situations are actively avoided, require the presence of a companion, or are endured with intense fear or anxiety.
D. The fear or anxiety is out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context.
E. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.
F. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
G. If another medical condition (e.g., inflammatory bowel disease, Parkinson's disease) is present, the fear, anxiety, or avoidance is clearly excessive.
H. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder—for example, the symptoms are not confined to specific phobia, situational type; do not involve only social situations (as in social anxiety disorder): and are not related exclusively to obsessions (as in obsessive-compulsive disorder), perceived defects or flaws in physical appearance (as in body dysmoφhic disorder), reminders of traumatic events (as in posttraumatic stress disorder), or fear of separation (as in separation anxiety disorder).

Note: Agoraphobia is diagnosed irrespective of the presence of panic disorder. If an individual's presentation meets criteria for panic disorder and agoraphobia, both diagnoses should be assigned.

Treatment
In case of acute anxiety symptoms or concomitant panic attack, benzodiazepines with a short or short-medium half-life can be used, e.g. alprazolam, clonazepam, lorazepam.
For long-term treatment, antidepressants are used. Although SSRIs are considered the first choice drugs in PAD and agoraphobia, TCAs (in particular clomipramine and imipramine) are even more effective, but they are used as a second option for they have greater side effects. For both categories, what has been said for anxiety disorders in general applies: start with a low dose checking for tolerability and then gradually increase to the effective dose in order to minimize paradoxical effects.
In addition to drug therapy, psychotherapy can be set up, whose orientation generally has a cognitive-behavioural approach.

5.1.5.4 SPECIFIC (SIMPLE) PHOBIA

In psychiatry, "phobia" means that a normal stimulus, even harmless in itself, is experienced as a danger capable of triggering an exaggerated somatic, psychic and behavioural reaction in some individual. The fear that the individual feels is actual and present when they are exposed to the phobic stimulus and is at the same time mixed with feelings of repulsion and disgust.
The characteristics of the phobia are:

- Disproportion of fear compared to the actual situation
- Invasive nature of fear thoughts
- Inability to dismantle them with rational arguments, awareness of the unreasonableness or exaggeration of fears
- Intense anxious reaction induced by exposure to the phobic stimulus
- Tendency to establish avoidance behaviours

Epidemiology
Specific phobia has a lifetime prevalence of 7-12%, with a F:M ratio of 2:1 and with variability between countries. It typically has two peaks: the first in childhood, in most cases before the age of 12 and another in early adulthood. Phobias that arise in childhood tend to spontaneous remission; it tends to have a more prolonged course in females. For some phobias (e.g. dark, blood, thunderstorms) spontaneous remissions can occur.

Clinical presentation
Despite being some fear understandable and shared by many people around the world, phobias become pathological when the fear leads to avoidance behaviours that negatively affect the subject's quality of life. Avoidance behaviours will be more or less disabling, in relation to the diffusion of the feared objects and situations.
The mechanism of phobias consists in identifying a stimulus, which is loaded in cognitive terms with negative values and therefore with anticipatory anxiety, then when the patient is in the specific situation anxiety reaches a peak level (similar to panic loop described above).

Some examples of phobias are:
- Acarophobia: insects
- Acrophobia: heights
- Agoraphobia: open spaces
- Brontophobia: thunder
- Claustrophobia: closed spaces
- Ereuthophobia: blushing
- Ochlophobia: crowd
- Pathophobia: diseases
- Rupophobia: dirty
- Thanatophobia: death
- Sitophobia: food
- Xenophobia: foreigners
- Zoophobia: animals

DSM-5 diagnostic criteria:

A. Marked fear or anxiety about a specific object or situation (e.g., flying, heights, and animals, receiving an injection, seeing blood).

Note: In children, the fear or anxiety may be expressed by crying, tantrums, freezing, or clinging.

B. The phobic object or situation almost always provokes immediate fear or anxiety.
C. The phobic object or situation is actively avoided or endured with intense fear or anxiety.
D. The fear or anxiety is out of proportion to the actual danger posed by the specific object or situation and to the sociocultural context.
E. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.

F. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
G. The disturbance is not better explained by the symptoms of another mental disorder, including fear, anxiety, and avoidance of situations associated with panic-like symptoms or other incapacitating symptoms (as in agoraphobia): objects or situations related to obsessions (as in obsessive-compulsive disorder); reminders of traumatic events (as in posttraumatic stress disorder); separation from home or attachment figures (as in separation anxiety disorder); or social situations (as in social anxiety disorder).

Treatment
In order to control symptoms, anxiolytics can be administered in the case of acute anxiety. On some occasions, beta-blockers may be indicated too.
However, the principal therapy is not pharmacological: exposures according to the principles of cognitive-behavioural therapy with the cognitive restructuring of the meanings pathologically attributed to the phobic stimulus and gradual exposures to progressively reduce the intensity of anxiety and gradually let the patient recover.

5.1.5.5 SOCIAL ANXIETY DISORDER (SOCIAL PHOBIA)

Social Anxiety Disorder It is characterized by a marked and persistent fear of social situations of interaction or in which a service must be provided, in which the subject is exposed to possible (negative) judgment by others.

Shyness is not synonymous with social phobia: shyness consists of being too self-conscious, it is a condition limited to the present moment but once the situation is overcome, the subject does not preclude subsequent situations. It can be present in some periods of childhood and is quite common in adolescence, then in most people, shyness decreases over time.

Epidemiology
It is a condition that markedly interferes with social relationships, it has a prevalence of 3-13%. It has an early onset, between 15-30 years. The incidence is higher in women than in men.

Risk factors seem to be the female gender, positive family history for social phobia, shyness or a tendency to behavioural inhibition in early childhood.

Comorbidities
Social phobia frequently occurs with alcohol, substance abuse, and depression.

Clinical presentation
Individuals with social phobia feel embarrassed during social situations and worry that anxiety symptoms (eg. flushing, sweating, and tremor) may reveal their state of discomfort to others. All this leads the patient to create impediments and obstacles in their daily life, isolating themselves from social situations, implementing avoidance strategies or delegating to others. During exposure to feared situations, there are marked neurovegetative manifestations such as palpitations, dizziness, redness, tremors, sweating, and hot flashes.

The most frequently feared social and performance situations in social phobia: conversation, public speaking, participating in small groups, eating, drinking or writing in public, talking to people who have an authority role, attending a party.

Specific subtypes of social phobia can be distinguished:

- Specific social phobia: it is an anxiety limited to one or two isolated situations; it is characterized by anticipatory anxiety.
- Generalized social phobia: anxiety is extended to almost all interpersonal situations, interpersonal difficulties and behavioural inhibition are constant. The subjects implement behaviours of referral, avoidance, renunciation and withdrawal towards interpersonal relationships. It is associated with paranoid and schizotypal personality structures (Cluster A).

Complications include:

- Social withdrawal and impairment of school or work performance, with subsequent development of feelings of inadequacy and inferiority;
- Substance abuse: alcohol (in 10-20%), anxiolytics and cannabinoids;
- Depressive syndrome: secondary demoralization, risk of suicide.

DSM-5 diagnostic criteria:

A. Marked fear or anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others. Examples include social interactions (e.g., having a conversation, meeting unfamiliar people), being observed (e.g., eating or drinking), and performing in front of others (e.g., giving a speech).

Note: In children, the anxiety must occur in peer settings and not just during interactions with adults.

B. The individual fears that he or she will act in a way or show anxiety symptoms that will be negatively evaluated (i.e., will be humiliating or embarrassing: will lead to rejection or offend others).
C. The social situations almost always provoke fear or anxiety.
D. Note: In children, the fear or anxiety may be expressed by crying, tantrums, freezing, clinging, shrinking, or failing to speak in social situations.
E. The social situations are avoided or endured with intense fear or anxiety.
F. The fear or anxiety is out of proportion to the actual threat posed by the social situation and to the sociocultural context.
G. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.
H. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
I. The fear, anxiety, or avoidance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.
J. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder, such as panic disorder, body dysmoφhic disorder, or autism spectrum disorder.
K. If another medical condition (e.g., Parkinson's disease, obesity, disfigurement from bums or injury) is present, the fear, anxiety, or avoidance is clearly unrelated or is excessive.

<u>Specify if:</u>

Performance only: If the fear is restricted to speaking or performing in public.

<u>Differential diagnoses:</u>

- Agoraphobia: avoidance of situations in which it would be difficult to receive help;

- Depression: social withdrawal and loss of confidence, but there was normal premorbid social functioning;
- Body dysmorphism;
- Cluster A Personality Disorder (where there is voluntary social withdrawal with egosynthony for interpretation and self-reference).

Treatment

The best treatment of social phobia involves a multidisciplinary approach, in which both pharmacotherapy and psychotherapy are used. Symptomatic drugs used are short half-life benzodiazepines (e.g. alprazolam, clonazepam) while drugs with curative purposes are antidepressants (mainly SSRIs, venlafaxine). In case of performance anxiety, beta-blockers can be used just before the phobic situation, e.g. atenolol 50-100 mg or propranolol 20-40 mg. Cognitive-behavioural psychotherapy, relaxation techniques and exposure exercise complete the treatment.

5.1.5.6 OTHER ANXIETY DISORDERS

SEPARATION ANXIETY DISORDER

Separation Anxiety Disorder is a typical condition of the child, burdened by excessive anxiety evoked by the separation from a parental figure. This condition is characterized by excessive sensitivity to separation with an intense anxious component, which interferes in the activities of daily life and with the normal development of the child.

SELECTIVE MUTISM

Selective Mutism is characterized by a persistent inability of the patient, typically a child, to communicate verbally in certain social life contexts that are selectively perceived as threatening (e.g. school). Conversely, the child normally talks at home with family members, such as siblings. Sometimes patients do not even speak in the family context if there are friends or relatives from outside the close family unit (e.g. grandparents, uncles, cousins).

SUBSTANCE/MEDICATION-INDUCED ANXIETY DISORDER

Substances such as anxiolytics, cannabinoids, alcohol which can give, after abrupt suspension, an anxious condition. So it is essential to adequately investigate the patient’s complete history.

5.2 SOMATIC DISORDERS

Introduction

The process of somatisation is defined as the tendency to experience, conceptualise or communicate psychological conditions or content through bodily sensations, functional modifications or somatic metaphors. It relates to all those situations in which the body occupies the whole space of communication and becomes the sole vehicle for transferring psychic messages. Body language not only participates and amplifies emotions but also can completely replace them.

This definition encompasses the complex and varied mechanisms that can be brought into play by patients who complain of physical complaints that cannot be explained from an organic point of view.

Before the patient can be included in one of the disorders of the somatisation phenomenon the following criteria have to be fulfilled:

- The presence of an underlying medical condition must be excluded;
- Even if a related medical condition exists, the intensity of the symptoms must not be proportionate to it.
- There are no demonstrable physiopathological mechanisms capable of explaining the symptoms.

5.2.1 SOMATIC SYMPTOM DISORDER (SSD)

Definition

Somatic Symptom Disorder is characterized by multiple and recurrent somatic complaints, lasting for years, for which medical intervention is sought; it has a chronic course, can lead to drug abuse, disability and iatrogenic illness.

The somatic symptoms must be associated with at least one of these psychological or behavioural responses:

- Excessive thoughts regarding the severity of the symptoms;
- High or persistent levels of anxiety;
- Excessive time and energy spent on concerns about health status.

Epidemiology

SSD is more frequent in the female population where it reaches a lifetime prevalence of 2%, whereas men's prevalence is less than 0.2%. There is a tendency towards familiarity (10-20% of female relatives of individuals with the disease are affected).

Diagnostic and clinical criteria

SSD is similar in its basic clinical features to the so-called Briquet syndrome, a homogenous form of hysteria characterized by multiple somatic symptoms and a chronic course. All patients with SSD have complicated medical histories. Any bodily organ or disorder can become a target of the somatisation process (abdominal pain, menstrual problems and headache are the most frequently occurring symptoms).

The most peculiar aspect in the SSD clinic is the dramatic, exaggerated and emotionally charged way in which the patient presents his or her history and the discomforts related to his or her symptoms.

The patient appears vindictive and accusatory towards the health care organization that has not been able to find a solution to the suffering produced by all her physical symptoms. The patient is often a woman who has recently given up her job and declares that she is unable to carry out her domestic activities. Marital relationships are described as highly unsatisfactory and the illness makes emotional relationships even worse. Sexuality is described as lacking in gratification. The DSM-5 definition requires only one body symptom that is distressing or disruptive to daily life and lasts at least 6 months. One of the following psychological or behavioural responses is also required (**Box 1**):

- Disproportionate thoughts about the severity of symptoms;
- Persistent high level of anxiety about the symptoms;
- Too much time and energy spent worrying about health.

In DSM-IV a total of 8 physically unexplained symptoms taken from four different symptom groups was required, of which at least 4 had pain and 2 had gastrointestinal symptoms.

Aetiology

Sociocultural, biological and psychodynamic factors are involved in the aetiology of SSD that interact or promote the establishment of a pathological personality profile and the development of other disorders, especially depressive and anxiety disorders. As regards the first factor, an association is recognised with:

- low socio-cultural level;
- childhood development in a family with subjects prone to somatisation;
- relationship with parents who were only capable of providing emotional care during states of illness;
- Health culture and practice that tends to privilege illness behaviour rather than the psychological expression of illness and therefore selects symptoms of a somatic nature.

From a biological point of view, SSD is interpreted as neurophysiologically determined by an abnormal lowering of the general threshold level to various stimuli. Thus, it is the experience of somatosensory amplification that determines a cognitive alteration of signal analysis.

5.2.2 ILLNESS ANXIETY DISORDER

Box 1: Diagnostic criteria for Somatic Symptom Disorder according to DSM-5

A. One or more somatic symptoms that are distressing or result in significant disruption of daily life.

B. Excessive thoughts, feelings, or behaviors related to the somatic symptoms or associated health concerns as manifested by at least one of the following:

1. Disproportionate and persistent thoughts about the seriousness of one's symptoms.
2. Persistently high level of anxiety about health or symptoms.
3. Excessive time and energy devoted to these symptoms or health concerns.

C. Although any one somatic symptom may not be continuously present, the state of being symptomatic is persistent (typically more than 6 months).

Definition

Illness anxiety disorder (IAD) takes the form of the pervasive belief and worry that one has or will have a serious illness whose origin is not discovered or excessive concern about one's health status. Somatic symptoms are not present, or if present are of mild intensity. This belief and/or fear is manifested through an unrealistic interpretation of the presumed physical symptoms.

Epidemiology

Prevalence estimates of IAD are based on those of DSM-3 and DSM-IV for the diagnosis of hypochondria. IAD is frequently observed in general practitioners' offices, where the prevalence of IAD in the patient population is about 10%. There is no difference between men and women; onset is more common during the third to fourth decade of life and in the elderly.

Clinical and diagnostic criteria

As in other SSD, the basic diagnostic condition is the absence of any organic pathology underlying the symptomatology that can fully justify the patient's state of mind, worries or beliefs. (Box 2)

Hypochondriacal symptoms may accompany other psychiatric disorders (major depression, schizophrenia) or be a temporary response to conditions of existential stress. The patient with IAD complains of physical symptoms, which, although caused by some organic disorder, are often exaggerated in their consequences, but above all are interpreted as caused by a serious illness that no doctor has yet been able to diagnose.

The symptoms affect the whole body and all organs and are expressed through pain and complaints in the heart or gastrointestinal tract. Headaches suggest tumours or aneurysms, mild arrhythmias suggest an impending heart attack, asthenia suggests AIDS. The symptomatology is chronic and the patient moves to the health care environment in the belief that some investigation has been overlooked or that he will finally find the doctor who can cure him.

Aetiology

The expression of the somatic symptom is the expression of a mental conflict, the thinking in IAD is more pervasive and pathological than in other forms of somatisation. The theatre where the hypochondriac plot unfolds is the entire internal world. Freud regarded hypochondria as a disinvestment of interest and vital energy from objects to the external world. The preoccupation with diseased organs represents the equivalent of anxiety in relation to strongly aggressive and destructive internal experiences. It is as if the patient were saying "I am afraid that someone in my body wants to harm and destroy me".

Box 2: Diagnostic criteria for Illness Anxiety Disorder according to DSM-5

- **A.** Preoccupation with having or acquiring a serious illness.
- **B.** Somatic symptoms are not present or, if present, are only mild in intensity. If another medical condition is present or there is a high risk for developing a medical condition (e.g., strong family history is present), the preoccupation is clearly excessive or disproportionate.
- **C.** There is a high level of anxiety about health, and the individual is easily alarmed about personal health status.
- **D.** The individual performs excessive health-related behaviors (e.g., repeatedly checks his or her body for signs of illness) or exhibits maladaptive avoidance (e.g., avoids doctor appointments and hospitals).
- **E.** Illness preoccupation has been present for at least 6 months, but the specific illness that is feared may change over that period of time.
- **F.** The illness-related preoccupation is not better explained by another mental disorder, such as somatic symptom disorder, panic disorder, generalized anxiety disorder, body dysmorphic disorder, obsessive-compulsive disorder, or delusional disorder, somatic type.

5.2.3 CONVERSION DISORDER

Definition

Conversion disorder corresponds to what used to be called hysterical neurosis. The core of this disorder is the patient's use of a physical symptom-forming mechanism, which consists in transferring unacceptable drives or instincts, desires or affections to the body (conversion) via voluntary nerve pathways. In this way, the unpleasant psychic charge of the conflict is removed.

Epidemiology

Conversion disorder is on the decline compared with the 19th and early 20th centuries. The prevalence among general hospital patients is high (ranging from 5 to 10%); in psychiatric wards this percentage drops considerably. Conversion disorder appears in both adolescence and early adulthood. It is more frequent in the female population, but there are two populations in which the prevalence in males is high: among victims of accidents at work and in the military. A low sociocultural level and ethno-cultural factors also play a role.

Clinical and diagnostic criteria

The symptoms presented by the patient usually mimic physical neurological diseases, i.e. of the sensory motor area. The diagnosis is complicated by the fact that the conversion disorder overlaps with an objective organic condition. This determines two phenomena: the first is a difficulty in differentiating the psychic quota present in the individual; the second is that often the presence of the theatrical and histrionic psychological characteristics of the patient with a conversion disorder can lead to an underestimation of possible organic aetiologies. (Box 3)

The symptomatology may have subacute characteristics, with a chronic course, or acute and dramatic (hysterical crises) with resolution of the symptoms themselves. In the latter case, we refer above all to epileptic crises of hysterical origin or to crises that are famous, but nowadays have become very rare, such as Charcot's *arc de cercle*.

It is necessary to remember that in conversion disorder, it is not possible to find a correspondence between an anatomical distribution of the venous pathways and the symptoms complained of by the patient; in fact, the latter are the expression of the idea of the disorder that the patient has constructed fantastically or through a process of imitation.

A feature that was thought to play a diagnostic role in the past was Janette's so-called *belle indifference*: in these cases, the patient appears unconcerned about the drama and severity of the symptoms.

Aetiology

On the study of hysteria, Freud built the basis of the theory and practice of psychoanalysis and the term conversion was introduced by Freud to explain the mysterious leap from the psychic to the somatic. The organic symptom becomes the representation of different types of drives, affections or instincts that are removed and rendered unconscious, as censorial or inhibitory forces (superego) determine a conflictual situation and make them incompatible with the individual's consciousness. Through somatisation (primary advantage) the subject gets rid of the conflict and therefore of the anguish produced by it and satisfies in a metaphorical way the removed aggressive, sexual drives or conflict (secondary advantage), through a physical representation.

Box 3: Diagnostic criteria for Conversion Disorder according to DSM-5

- **A.** One or more symptoms of altered voluntary motor or sensory function.
- **B.** Clinical findings provide evidence of incompatibility between the symptom and recognized
- **C.** Neurological or medical conditions.
- **D.** The symptom or deficit is not better explained by another medical or mental disorder.
- **E.** The symptom or deficit causes clinically significant distress or impairment in social, occupational, or other important areas of functioning or warrants medical evaluation.

5.2.4 FACTITIOUS DISORDER

Factitious disorders are characterised by physical or psychic symptoms that are intentionally produced or simulated in order to assume the role of a sick person. The main feature of this disorder is the intentional production of behaviours or symptoms of a physical or psychic disorder. The subject may adopt subjective complaints (abdominal pain in the absence of specific symptoms or falsification of objective signs such as manipulation of a thermometer to create the illusion of fever).

Fictitious disorders must be distinguished from acts of simulation in which the subject produces the symptoms intentionally, but is seeking a secondary benefit (avoiding work obligations or avoiding being selected for stressful tasks or roles).

Epidemiology

Factitious diseases are very frequent; it has been calculated that more than 5% of contacts between doctor and patient occur for these reasons.

Clinical and diagnostic criteria

Individuals with a bogus disorder may seek treatment for themselves or another person after deliberately causing the injury or illness. Diagnosis requires demonstration that the individual is deliberately faking-causing signs or symptoms of illness or injury in the absence of obvious external benefit (box 4). Factitious disorder has similarities to substance-related disorders, nutrition and eating disorders and impulse control disorders, as well as to other disorders related to both the persistence of disturbed behaviour and deliberate efforts to conceal such behaviour by deception. The diagnosis of factitious disorder emphasises the objective finding of a falsification drawing symptoms of illness, without drawing inferences about the possible international underlying motivation.

Patients seem to be resistant to undergo a psychiatric examination, which does not yield encouraging results. Affected persons often involve family members, health and social workers. The clinical history invented by the patient is usually credible and plausible, although the details are often vague and inconsistent. A common aspect of the factitious disorder is that patients undergo endless examinations and even invasive and disturbing investigations, denoting a kind of self-harm.

Course and prognosis of somatic symptom disorders and related disorders

The disorders that appear in the group of SDS and related disorders tend to have a chronic course, whether the symptoms are long-lasting or present periods of remission of varying lengths and then reappear. In conversion disorder, crises (usually of short duration) become chronic in only 10% of cases. In general, it is possible to say that acute onset is linked to a better prognosis, whereas subtle onset is a slow and complex establishment of the various somatisation symptoms that expose the patient to very serious risks.

The prognosis is linked to the patient's personality traits and the type of psychological conflict that characterises him or her; equally important is the presence of a concomitant organic pathology. Linked to this picture of illness are affective disorders, which are often associated not only with the physical symptoms but also with the psychological symptoms of the patient.

Factitious Disorder by proxy

A specific form of Factitious Disorder is the Factitious Disorder by proxy.

The essential characteristic is 'the deliberate production or simulation of physical and/or psychic signs or symptoms in another person who is in the care of the subject'. Typically, the victim is a young child (usually up to 5 years old) and in 90% of cases, the perpetrator is the mother.

They appear very distant from the image of an abusive mother, on the contrary, they seem to be caring, anxious for the health of their children, very cooperative and grateful towards the doctors, which encourages the latter to investigate more and more the causes of these symptoms. The figure of the father is generally marginal; he is usually absent or mostly passive in family life.

Box 4: Diagnostic criteria for Factitious Disorder (Imposed on Self) according to DSM-5

- **A.** Falsification of physical or psychological signs or symptoms, or induction of injury or disease, associated with identified deception.
- **B.** The individual presents himself or herself to others as ill, impaired, or injured.
- **C.** The deceptive behavior is evident even in the absence of obvious external rewards.
- **D.** The behavior is not better explained by another mental disorder, such as delusional disorder or another psychotic disorder.

Symptoms are usually not characteristic of known illnesses and this confuses paediatricians and other clinicians and prompts them to investigate further. It is usually a long time before clinicians start to consider the idea that the patient's illness is caused by the caregiver.

Box 5: Diagnostic criteria for Factitious Disorder by proxy according to DSM-5

A. Intentional induction or falsification of physical or psychological signs or symptoms
B. The individual presents themselves as ill, impaired or injured to others
C. The deceptive behavior persists even in the absence of external incentives or rewards
D. Another mental disorder does not better explain the behavior

The methods used to create symptoms in victim patients are heterogeneous and often cruel.

The way in which the syndrome manifests itself varies greatly. In some cases, the caregiver may make false accusations of physical and/or sexual abuse of their child, causing the child to suffer the pain of being subjected to detailed questioning, and sometimes the caregiver may alter the results of their child's tests, for example by contaminating urine samples with poisons, herbicides or other toxic substances. Physical attacks included pinpricks on the face and body, facial injuries from tools or nails, and suffocation by pressing a hand or pillow to the face. Other equally dangerous physical attacks were voluntary undernutrition and a dirty and neglected home environment, induction of epileptic seizures or loss of consciousness.

Treatment of somatic symptom disorders and related disorders

The basic assumption to refer to in formulating an action strategy is that all patients with SSD and related disorders have the belief that a physical disorder is at the origin of the complained symptoms and therefore lack the ability to desomatize the removed effects and conflicts. It is for this reason that the patient appears dissatisfied when he/she is told that he/she has nothing, in fact he/she gets irritated and thinks that he/she has not been taken into consideration. This is where the psychic defences in somatisation and the series of medical pathways begin to strengthen. The doctor, therefore, must:

- Establish a sincere relationship of pure understanding. In the diagnostic period, it is fundamental to build a relationship of trust both through a precise execution of the clinical investigations and through an attitude of understanding and not of disqualification.

- Collection of an existential anamnesis with the aim of placing the appearance of physical symptoms in relation to very important existential and stressful events (bereavements, painful experiences, sentimental disappointments, etc.).

- Highlighting, whenever possible, psychological symptoms or discomforts that were already present before or even concomitantly with the appearance of the physical symptoms.

- Restitution of the medical diagnosis with hypotheses of objective connections. This is the most delicate phase. It should not be communicated 'you have nothing' but, for example, 'everything is quite well and it is difficult to explain all your complaints with the results of these tests'. The doctor will respond with some examples from common experience that can show how fears, anxiety, depression and anger are always accompanied by physical experiences. If the heart beats fast during unexpected events, this is because there are nerve endings in the heart that start in the brain. The answer that will often be given will be "but I am not anxious or depressed", this is the time to move on to the next point.

- Returning hypotheses of subjective connections. Now one has to use the information gathered earlier. It is important to offer these connections to the patient as hypotheses. Therefore, it is necessary to use "you are right, he does not seem to me at this moment anxious or depressed, however it is curious that the disorders started shortly after his mother died. I think this is very important emotionally". It is important to remember not to force the patient's defences.

- Referral to psychiatric specialist. If the doctor has succeeded in gaining the patient's trust, a sentence such as "I think it might be worthwhile to try the psychological route as well" will be readily accepted by the patient.

- Psychiatric treatment. Pharmacotherapy is necessary in the presence of co-morbidity with other psychiatric pathologies such as mood and anxiety disorders: however, it is psychotherapy that is the preferred option. Its aim is to clarify the dynamics and the psychic facts that have determined the somatisation process, to build with the patient the mental equipment with which he can face conflicts and life events in a different way.

5.3 OBSESSIVE-COMPULSIVE AND RELATED DISORDERS

Obsessive-Compulsive Disorder (OCD) has been considered as part of the Anxiety Disorders chapter up to the fourth edition of the DSM (DSM IV-TR), while from the fifth edition (DSM- 5) it is placed in a separate chapter. The nosographic autonomy of this disorder depends on the fact that the anxious manifestations, even if present, would be secondary and dependent on the obsessive contents. A group of conditions related to it from a clinical, epidemiological and sometimes etiopathological perspective is included in the DSM chapter about obsessive-compulsive disorder.

The DSM-5 "Obsessive-compulsive and related disorders" chapter currently includes:

- Obsessive-Compulsive Disorder
- Obsessive-Compulsive and Related Disorder Due to Another Medical Condition
- Substance / Medication-Induced Obsessive-Compulsive and Related Disorder
- Other Specified Obsessive-Compulsive and Related Disorder
- Body Dysmorphic Disorder
- Hoarding Disorder
- Trichotillomania (Hair-Pulling Disorder)
- Excoriation (Skin-Picking Disorder)

5.3.1 OBSESSIVE-COMPULSIVE DISORDER

Definition

The double etymology of the term "obsessive-compulsive" portrays the nature of the disorder immediately: obsession derives from the Latin *"obsidere*" which means to besiege, while "compulsive" derives from the Latin verb "*compellere*" or to force. The subject affected by this disorder is on one hand surrounded, pursued, by his obsessions and on the other, compelled, forced to carry out compulsions.

Epidemiology

Until the 1990s, obsessive-compulsive disorder was considered a rare disease. Instead, recent epidemiological studies have significantly revised previous estimates. Today, this disorder is in 4th place regarding psychiatric pathologies, preceded only by phobias, substance-related disorders, and major depression.

The lifetime prevalence of OCD is between 0.3 and 3.5%, with a mean prevalence of approximately 2%.

The distribution in adults is the same in males and females, while it seems to affect boys more than girls in adolescence. The average age of onset is about 20 years (66% of cases), slightly earlier in males (19) than in females (22). A second peak of onset occurs at 35 years (15% of cases). Late onset appears rarer, and any underlying organic pathologies must be carefully investigated in such cases. Obsessive thoughts are described in a high percentage (57%) of women with postpartum depression.

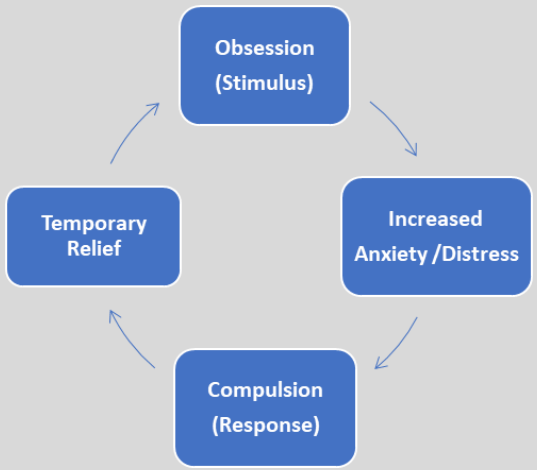
Etiopathogenesis

Obsessive-Compulsive Disorder appears to be a multifactorial disease. Biological and psychosocial factors contribute to the pathogenesis of the disorder. Studies in different research habits support this hypothesis:

- *Genetic studies:* First-degree relatives have a 12% overall risk of developing OCD, six times greater than the general population. The concordance between non-twin siblings / dizygotic twins is approximately 50%, reaching 85% in homozygous twins.

- Neuroanatomy: brain imaging studies have shown an increase in metabolic activity in some cortical regions (orbitofrontal cortex) and subcortical regions (caudate nucleus, dorsomedial thalamus). This increase in activity appears to be reversible after drug or behavioural therapy.
- *Serotonin and Noradrenaline*: the finding of reduced levels of serotonin metabolites in the cerebrospinal fluid of patients with OCD combined with the evidence of clinical efficacy from drugs that act on the serotonin system (SSRI, SNRI, TCA), seems to indicate a role of this neurotransmitter in the pathogenesis of the disorder. The high frequency of OCD symptoms in patients with basal ganglia alterations and the antipsychotic response of some forms of OCD resistant to antidepressants seem to indicate the involvement of the neurotransmitter dopamine.
- *Behavioural factors*: from a behavioural point of view, obsessions can be considered as conditioned stimuli. A neutral stimulus is associated, by classical conditioning, with an event that produces anxiety or suffering. From that moment, the thought alone will be able to cause anxiety or discomfort until it becomes a real obsession. Always according to a behavioural model, the compulsion is established when the subject identifies an action or thought that is able to reduce an unpleasant sensation (i.e. tension, anxiety). The subject will repeat the action/thought as a strategy to avoid the unpleasant sensation and gradually, this action/thought will take on the characteristics of an indispensable ritual, a compulsion (Box 1).

Box 1: the OCD "loop"



Clinical presentation

Diagnostic criteria include persistent and recurring thoughts/images (obsessions) or repetitive behaviours (compulsions). Commonly, the patient manifests both, however in some cases only obsessions are be present. Compulsions alone are much rarer, typical of protracted illness pictures, in which the patient automatically carries out behaviours unrelated to the content of thought. (Box 3)

Obsession: it can be an idea, an image, a fear, an impulse. It is a mental content; it cannot be objectified clinically. Obsessions can have different contents (Box 2a) and can be described by some characteristics:

- Persistence/recurrence of the obsessive content and degree of impairment of the patient's functioning
- Egodistonia: obsession produces discomfort, is experienced as intrusive and extraneous
- Invincibility: does not depend on or respond to the will of the patient
- Criticism/Insight: the patient tends to recognize it as a product of his own mind
-

Compulsion: repetition of an action or mental action that the subject carries out in response to an obsession following a rigid scheme (Box 2b). Although sometimes they may only be mental, in most cases they are actions, behavioural manifestations that can be described by:

- Repetitiveness: the actions are stereotyped and repeated according to a precise pattern.
- Purpose: compulsions are carried out in order to reduce an unpleasant feeling or in order to prevent it.
- -Intentionality: Actions are carried out deliberately; they are not involuntary.

Box 2a: most common obsessive contents:

- *Aggressive and sexual obsession*: the patient is afraid of being able to carry out or have already carried out deplorable or harmful actions for himself or for others.
- *Obsessions of symmetry / perfection*: it can concern every area of life of the subject, from objects to his own body. Everything must be precisely arranged or organized (alphabetical, chromatic, symmetrical ...)
- *Obsessions of contamination*: the patient is worried that he may contract infections or come into contact with harmful substances. Sometimes the fear does not concern only physical contamination but also symbolic (fear of coming into contact with evil or the devil)
- *Obsessions related to doubt / control*: the patient fears that, in the absence of repeated checks, situations or behaviors could lead to unpleasant consequences
- *Unrealistic, magical, and superstitious beliefs*: the patient is convinced that specific actions or thoughts can influence the outcome of events even when it is clear that there is no causal relationship between the two.

Box 2b: most common types of compulsion:

- *Control Compulsions*: repetitive and excessive control of actions, objects or situations. Typically related to doubt obsession
- *Compulsions of washing and cleaning*: frequent and excessive washing of parts of the body, objects or environments. Related to contamination obsession.
- *Compulsions of order*: reorganization and arrangement of objects / environments according to rigid pre-established schemes. In response to obsessions of order / symmetry
- *Counting Compulsions*: the patient carries out counts, lists or mental operations. Usually in response to superstitious obsessions

Box 3: Diagnostic criteria for obsessive-compulsive disorder according to DSM-5

A. Presence of obsessions, compulsions, or both:
Obsessions are defined by (1) and (2):
1. Recurrent and persistent thoughts, urges, or images that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress.
2. The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (ie, by performing a compulsion).
Compulsions are defined by (1) and (2):
1. Repetitive behaviors (eg, hand washing, ordering, checking) or mental acts (eg praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.
2. The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent or are clearly excessive.
Note: Young children may not be able to articulate the aims of these behaviors or mental acts.

B. The obsessions or compulsions are time-consuming (eg, take more than 1 hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication) or another medical condition.

D. The disturbance is not better explained by the symptoms of another mental disorder (eg, excessive worries, as in generalized anxiety disorder; preoccupation with appearance, as in body dysmorphic disorder; difficulty discarding or parting with possessions, as in hoarding disorder; hair pulling, as in trichotillomania [hair-pulling disorder]; skin picking, as in excoriation [skin-picking] disorder; stereotypies, as in stereotypic movement disorder; ritualized eating behavior, as in eating disorders; concern with substances or gambling, as in substance- related and addictive disorders; concern with having an illness, as in illness anxiety disorder; sexual urges or fantasies, as in paraphilic disorders; impulses, as in disruptive, impulse-control, and conduct disorders; guilty ruminations, as in major depressive disorder; thought insertion or delusional preoccupations, as in schizophrenia spectrum and other psychotic disorders; or repetitive patterns of behavior, as in autism spectrum disorder).

Specify if:
With good or fair insight: The individual recognizes that obsessive-compulsive disorder beliefs are definitely or probably not true or that they may or may not be true.
With poor insight: The individual thinks obsessive-compulsive disorder beliefs are probably true.
With absent insight / delusional beliefs: The individual is completely convinced that obsessive-compulsive disorder beliefs are true.
Specify if:
Tic-related: The individual has a current or past history of a tic disorder.

Course

The onset of symptoms occurs suddenly in most patients, sometimes preceded by a stressful event (i.e. bereavement, pregnancy, brain injury). In a smaller number of patients, the onset appears more subtle, insidious, and gradual. In these cases, the patient will tend to hide the symptoms more frequently, deferring medical help requests even for several years.

The course of symptoms tends to have two main patterns: episodic (25% of cases), in which phases of well-being alternate with active phases of the disorder and chronic (75% of cases), in which the symptoms never entirely recede.

Obsessive-compulsive symptoms, especially in the chronic evolution, can have a stable or fluctuating course, with periods of partial remission alternating with a recurrence of symptoms.

Finally, in 10% of cases, the trend is progressive; this is the most severe clinical form, characterized by worsening of symptoms over time.

The impact of obsessive-compulsive disorder on the lives of those afflicted can be dramatic. Obsessions and compulsions can occupy a large part of the day, interfering with work, social, school and relational activities. In the most severe forms, the patient is wholly absorbed by the fears and rituals he puts in place to calm the resulting discomfort. In chronic states with a worsening trend, the patient can face a real cognitive impairment.

The onset of suicidal ideation is described in about half of OCD patients, while actual suicide attempts in about 25% of patients. The risk of suicide increases when depressive symptoms are associated with OCD.

Comorbidities

OCD can have several comorbidities, and these are the most frequent:

- Mood Disorders: Major Depression and Bipolar Disorder, up to 60% of cases. Mood disorders can precede OCD or be a consequence.
- Anxiety disorders: In particular, panic disorder and phobias, up to 70% of cases.
- Tourette's Syndrome: Up to 50% of sufferers also develop OCD
- Tic disorder: involuntary, afinalistic, intermittent movements can be present in up to 30% of patients with OCD.

Treatment

Treatment of obsessive-compulsive disorder is based on two main interventions: drug therapy and cognitive-behavioural therapy (CBT). The latter is to be preferred to the psychodynamic approach and psychoanalysis, towards which patients with this disorder seem to be refractory. It should be remembered that generally better results are obtained with the combination of drug therapy and behavioural therapy.

Pharmacological therapy:

SSRI

The first line for the treatment of OCD is usually monotherapy with antidepressant drugs belonging to the category of SSRIs. The dosage range is comparable to that for the treatment of depressive episodes; however, the beneficial effect of these drugs on obsessive-compulsive symptoms is generally delayed. It usually takes at least 4-6 weeks of treatment to get the first results, with the maximum therapeutic benefit being achieved on average after 12 weeks of treatment. When there is a response to treatment, therapy should be continued for at least 2 years, possibly reducing the dosage to approximately 50-60% of the effective attack dose.

Other drugs

Among the non-SSRI antidepressants, clomipramine, an antidepressant drug belonging to the class of tricyclics (TCA), is the one with the greatest selectivity on serotonin re-uptake. It was the first drug approved for the treatment of OCD; however, with the advent of SSRIs with fewer side effects, it became a second choice in treating this disorder.

If drug treatment with SSRIs or clomipramine is ineffective, combination with other drug categories can be evaluated. Generally, drugs used to augment SSRI / clomipramine therapy include stabilizers (valproate, carbamazepine), second-generation antipsychotics (risperidone, olanzapine, aripiprazole), benzodiazepines, beta-blockers (pindolol).

Venlafaxine, an antidepressant drug belonging to the SNRI category, has been shown to be effective in the treatment of OCD.

Non-pharmacological therapy

Cognitive Behavioural Therapy (CBT)

Among the psychological therapies, the one that has proved most effective in obsessive-compulsive disorder is cognitive-behavioural therapy. CBT has been shown to be at least as effective as drug therapy in treating OCD. The main approach of this technique is exposure and response prevention (ERP). A treatment lasting 15-20 weeks, once a week, is generally recommended. The outpatient meetings are supplemented by exercises that the patient carries out daily and independently. On the other hand, psychodynamic therapy is not recommended, while family therapy can help manage the conflict that often arises between the patient and the closest relatives due to the peculiar symptoms of the disorder.

5.3.2 BODY DYSMORPHIC DISORDER

The disorder is characterized by the patient's concern for one or more physical defects. These defects can only be imagined by the patient or, when present, are of modest entity. The patient's concern is, in both cases, excessive and can become invalidating.

Epidemiology

There is no clear epidemiological description of the disease. Patients affected by this disorder, in fact, tend to turn to various health professionals, in particular dermatologists and plastic surgeons, thus making diagnosis and epidemiological investigation difficult.

The prevalence of the disorder appears to be around 2.4% of the population, with a slight predominance of women. The number tends to increase within specific groups of patients, such as dermatological patients (9-15%) or patients who turn to cosmetic surgery (up to 16%).

Aetiology

It is not known. Comorbidity with mood disorders and OCD and the good chance of responding to antidepressant drugs suggest a role for serotonin in the disorder's pathophysiology.

The family, work, and social context seem to play a role, being the disorder more frequent in contexts in which a certain beauty stereotype is emphasized.

Clinical presentation

Patients may complain of concerns about defects in every possible location in the body. However, several studies have identified the skin, hair and nose as the most frequent locations, which in any case can vary over time. The worry can be more or less specific and intense, ranging from "less-than-perfect" to "unsightly". (Box 5)

The idea of having a physical defect produces a sense of discomfort and concern such as to induce the patient to carry out repetitive behaviours to control their appearance (directly or in the mirror) or attempts to conceal the alleged defect through make-up, clothes or accessories. In some patients, avoidance behaviours may develop and can lead to real social isolation. Up to 20% of patients attempt suicide. Concerning the course, the onset is more frequently placed in adolescence while the progress is generally chronic, with periods of greater intensity of worries alternating with periods of almost complete well-being.

Therapy

The most effective pharmacological approach sees antidepressant drugs belonging to the class of SSRIs and TCAs at the forefront. Anecdotally, some antipsychotics (pimozide) and monoamine oxidase inhibitors (MAOIs) have been shown to be effective. Since comorbidity with mood disorders and anxiety disorders is common, treatment should include specific therapy for these conditions as well. The timing of maintenance of the effective drug after the remission of symptoms is not known.

Surgical treatment of the real or perceived bodily anomaly is almost always doomed to failure and is accompanied by a high rate of litigation and complaints by the patient, dissatisfied with the outcome of the procedure.

Box 5: DSM-5 Criteria for Diagnosing Body Dysmorphic Disorder

A. Preoccupation with one or more perceived defects or flaws in physical appearance that are not observable or appear slight to others.

B. At some point during the course of the disorder, the individual has performed repetitive behaviors (ex, mirror checking, excessive grooming, skin picking, reassurance seeking) or mental acts (ex, comparing his or her appearance with that of others) in response to the appearance concerns.

C. The concern causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The appearance concern is not better explained by concerns with body fat or weight in an individual whose symptoms meet diagnostic criteria for an eating disorder.

Specify if:

With muscle dysmorphia: The individual is preoccupied with the idea that his or her body build is too small or insufficiently muscular. This specifier is used even if the individual is preoccupied with other body areas, which is often the case.

Specify if:

Indicate degree of insight regarding body dysmorphic disorder beliefs (eg, "I look ugly" or "I look deformed").

With good or fair insight: The individual recognizes that the body dysmorphic disorder beliefs are definitely or probably not true or that they may or may not be true.

With poor insight: The individual thinks that the body dysmorphic disorder beliefs are probably true.

With absent insight / delusional beliefs: The individual is completely convinced that the body dysmorphic disorder beliefs are true.

Box 6: Muscle Dysmorphia

It is a specific form of dysmorphic Disorder, which almost exclusively affects males. The patient is concerned that their body is not big and muscular enough. This worry can lead to strenuous workouts, weight lifting, or improper diets. Generally, the patient's awareness is low and to the possible consequences described for Dysmorphic Disorder, we can add the effects on the body of extreme training and particular nutrition.

5.3.3 HOARDING DISORDER

Originally, this disorder was considered a category of OCD; currently it is placed in a separate category, falling within the OCD-related disorders.

In hoarding disorder the patient buys or comes into possession of objects, generally of little or no value and cannot get rid of them. This behaviour can result in a progressive accumulation of objects, up to completely occupying the patient's living and living spaces.

The fear of getting rid of such objects is motivated by the belief that they may prove useful in some way in the future or by an excessive affective attachment to them.

Epidemiology

Hoarding Disorder affects approximately 4% of the general population. The patients who reach the doctor's attention are mostly women although, according to epidemiological studies, the problem is more common in males. The disorder is ubiquitous; no predisposing cultural factors have emerged. The accumulation of objects often begins in adolescence (11-15 years) and increasingly interferes in the following years, when the subject generally becomes more autonomous in the care of living environments.

Aetiology

Factors related to temperament and personality seem to play a role in the genesis of the disorder. Temperamental characteristics of indecision or dependent personality traits are described more frequently among the accumulators. From the genetic point of view, familiarity for accumulation disorders are present in 50% of the affected population. Specific markers on the long arm of chromosomes 4, 5, 17 have also been described, as well as polymorphisms in the COMT gene.

From a biological point of view, metabolic alterations in the occipital and posterior cingulate cortex have also been described.

Clinical presentation

The patient is convinced that the objects he accumulates may have some function in the future and for this reason, he cannot get rid of them. In other cases, the accumulator describes an extreme emotional bond to the object that cannot be broken. In both cases, there is an overestimation of the function or of the affective/effective value of what accumulates (Box 7).

Objects are often accumulated in an unorganized and passive way. In fact, the patient sometimes simply avoids choosing whether to get rid of the object or not.

Anything can be accumulated: books, clothes, cards, lists, magazines, letters etc.

Accumulation can go to extreme levels. Patients can literally fill their homes with materials of any kind, with serious health and safety consequences for themselves and others. Often this disorder results in social or legal problems. It is frequent that patients arrive at a progressive social isolation. Other times they are forced by the owners to abandon their homes for reasons of safety or decorum. Awareness of one's problem is generally low. Sometimes completely absent. In such cases there may be a delusional ideation concerning the usefulness or necessity of the accumulated objects. In three out of four patients, an anxiety or mood disorder is present in addition to hoarding disorder. The most common are major depression and social anxiety disorder. Often it is precisely the possible comorbidities that bring the patient to the doctor's attention

Treatment

From a pharmacological point of view, there is no standard approach. SSRIs, first-line drugs in the treatment of obsessive-compulsive disorder, instead had very low response rates in hoarding disorder (<20%), in other cases they had even negative response.

The approach that has been most effective to date is based on a cognitive-behavioural model; however, the CBT protocols used for OCD have proved ineffective.

The protocols currently used are therefore specific and include three main points: the acquisition of problem solving skills, decision-making and organization, gradual exposure (imaginative or live) to stressful stimuli with gradual prevention of the response and finally restructuring cognitive dysfunctional beliefs about the disorder.

Box 7: DSM-5 Criteria Box for Diagnosis of Hoarding Disorder

A. Persistent difficulty discarding or parting with possessions, regardless of their actual value.
B. This difficulty is due to a perceived need to save the items and to distress associated with discarding them.
C. The difficulty discarding possessions results in the accumulation of possessions that congest and clutter active living areas and substantially compromises their intended use. If living areas are uncluttered, it is only because of the interventions of third parties (ex, family members, cleaners, authorities).
D. The hoarding causes clinically significant distress or impairment in social, occupational, or other important areas of functioning (including maintaining a safe environment for self and others).
IS. The hoarding is not attributable to another medical condition (ex, brain injury, cerebrovascular Disease, Prader-Willi syndrome).
F. The hoarding is not better explained by the symptoms of another mental disorder (ex, obsessions in obsessive-compulsive disorder, decreased energy in major depressive disorder, delusions in schizophrenia or another psychotic disorder, cognitive deficits in major neurocognitive disorder, restricted interests in autism spectrum disorder).

Specify if:
With excessive acquisition: If difficulty discarding possessions is accompanied by excessive acquisition of items that are not needed or for which there is no available space.

Specify if:
With good or fair insight: The individual recognizes that hoarding-related beliefs and behaviors (pertaining to difficulty discarding items, clutter, or excessive acquisition) are problematic.
With poor insight: The individual is mostly convinced that hoarding-related beliefs and behaviors (pertaining to difficulty discarding items, clutter, or excessive acquisition) are not problematic despite evidence to the contrary.
With absent insight / delusional beliefs: The individual is completely convinced that hoarding-related

5.3.4 HAIR-PULLING DISORDER (TRICHOTILLOMANIA)

Hair pulling disorder, also known as trichotillomania, is a disorder related to OCD. It is a chronic condition that often leads to hair loss. The subject affected by this disorder repeatedly performs the gesture of pulling hair or body hair in order to relieve a state of increasing tension or for the sense of gratification that derives from it.

Epidemiology

Evaluating the real epidemiology of the disorder is not easy; the patient often feels ashamed and may not require the doctor's attention. About one third of patients wait more than a year before seeking medical attention.

Current estimates evaluate a distribution between males and females in a ratio of approximately 1 to 10 and a lifetime prevalence between 0.5 and 3.5% of the general population.

Aetiology

The aetiology appears to be multifactorial. Some polymorphisms in genes coding for serotonin receptors as well as morphological variations in the basal ganglia (putamen, lenticulated nucleus) have been investigated. Depressive symptoms, conditions of emotional stress, as well as childhood trauma have always been considered as important factors for the development of the disorder albeit there is no uniformity of thought in this regard.

Clinical presentation

The symptoms essentially consist of repeated pulling of hairs or body hairs that can affect all parts of the body with a preference for the scalp and face (eyelashes, eyebrows, and beard). The act of tearing is often preceded by a feeling of increasing tension, while subsequently the patient feels a certain sense of relief or satisfaction. (Box)

There are two main types of tearing:

- *Focus pulling:* the act is intentional and is carried out in response to the appearance of an unpleasant experience, such as a thought, an impulse or a bodily sensation.
- *Automatic pulling*: the act is unconscious, it occurs in the course of another activity, typically sedentary.

Often the two types of pulling alternate and can be succeeded by ingestion or chewing of the hair. Ingestion can complicate the situation leading to the formation of bezoars and intestinal obstruction / malnutrition. (Box 8)

The patient will often see areas of the scalp with sparse, broken hair at different stages of growth. The same can be said for eyelashes, eyebrows or other hairy areas.

The course appears to be highly variable. The disorder can have a chronic course or phases of temporary remission. The forms with the best prognosis are those that begin at a very young age (<6 years) while the adolescent forms tend to become chronic more frequently.

Therapy

Although there is no univocal consensus within the scientific community, the two most effective lines of treatment seem to be pharmacological and psychotherapeutic. From a pharmacological point of view, the first line of treatment includes antidepressants belonging to the class of SSRIs (fluvoxamine, citalopram) and SNRIs (venlafaxine), the use of local steroids, and antihistamines (Hydroxizine). Other proposed pharmacological strategies include the use of pimozide lithium salts, a first generation antipsychotic and opioid receptor antagonists such as naltrexone.

As far as psychotherapy is concerned, the literature data are scarce; the greatest effectiveness seems to derive from the psychodynamic approach.

Box 8: DSM-5 Criteria for Diagnosing Hair-Pulling Disorder

A. Recurrent pulling out of one's hair, resulting in hair loss.
B. Repeated attempts to decrease or stop hair pulling.
C. The hair pulling causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The hair pulling or hair loss is not attributable to another medical condition (eg, a dermatological Condition).
IS. The hair pulling is not better explained by the symptoms of another mental disorder
(eg, attempts to improve a perceived defect or flaw in appearance in body dysmorphic

5.3.5 EXCORIATION (SKIN-PICKING) DISORDER

This condition has been described since the late nineteenth century. Long called "dermatillomania" it found a precise definition only recently when it was placed in the DSM-5 among the obsessive-compulsive spectrum disorders.

The key feature that describes this disorder is recurrent picking of the subject's skin. This skin picking has the characteristics of a compulsion and can lead, in the long term, to serious tissue damage with the need for specific pharmacological treatments.

Epidemiology

The disorder has a prevalence of 1.4% in the general population, increasing to 12% in the adolescent population. In 75% of cases, the female sex is affected.

Aetiology

The aetiology is unclear. From a biological point of view, some form of neurochemical alteration has been hypothesized, in particular in the metabolism of serotonin, dopamine, and glutamate. From a psychological point of view, several hypotheses have been formulated: picking in adolescents could be a manifestation of anger towards parental figures. From a psychoanalytic point of view, skin picking would be seen as a form of autoeroticism. Finally, there is the hypothesis that excoriation is a mechanism for relieving stress. It should also be noted that often the onset of the disease coincides with the onset of dermatological conditions, such as acne. In this case, however, the teasing often continues even when the favouring dermatological condition resolves.

Clinical presentation

As with hair-pulling disorder, excoriation is often preceded by a sense of increasing tension and followed by a sense of relief. The most commonly affected site is that of the face. In other cases, the limbs, torso, fingers, scalp may be involved. Often, the patient turns over different areas to give the skin time to heal. Patients are generally highly embarrassed by the disorder and its aesthetic consequences. This discomfort can be accompanied by avoidance and social withdrawal or masking of the areas involved with makeup, clothes, and sometimes bandages. (Box 9)

The onset of the disorder can be placed in two phases, the first around the age of 14 while the second in adulthood, between 30 and 45 years. The diagnosis can be delayed: often, the affected person is not aware of this disorder and the possibilities of treatment and can turn to the doctor's attention when skin damage is irreversible. The course of the disorder appears to be fluctuating, with periods of remission and recrudescence.

Excoriation disorder can be disabling; most of those affected feel intense discomfort and embarrassment, implementing social avoidance behaviours. It can lead to the abandonment of school or of the workplace. The disorder can also lead to major tissue damage with the development of infections and scars that often require medical intervention, antibiotics, and even surgery.

Therapy

Although there are no real guidelines, the treatment of this condition mainly uses pharmacotherapy and psychotherapy, preferably in combination.

From a drug perspective, those found most effective in treating the disorder include SSRIs, opioid antagonists (naltrexone), and stabilizers, particularly lamotrigine.

As for psychotherapy, it appears that brief cognitive-behavioural therapy (CBT) may be an effective solution.

In some circumstances, mechanical prevention of picking utilizing aids or protective measures may help.

Box 9: DSM-5 Criteria for Diagnosing Excoriation (Skin-Picking) Disorder

A. Recurrent skin picking resulting in skin lesions.
B. Repeated attempts to decrease or stop skin picking.
C. The skin picking causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The skin picking is not attributable to the physiological effects of a substance (eg, cocaine) or another medical condition (eg, scabies).
E. The skin picking is not better explained by symptoms of another mental disorder (eg, delusions or tactile hallucinations in a psychotic disorder, attempts to improve a perceived defect or flaw in appearance in body dysmorphic disorder, stereotypies in stereotypic movement disorder, or intention to harm oneself in non-suicidal self-injury).

5.4 TRAUMA AND STRESS RELATED DISORDERS

The disorders grouped in this chapter have in common the exposure to a traumatic or stressful event as the foundational event in disorder development.

The psychological stress that follows a traumatic or stressful event varies from person to person. In some cases, some symptoms can be understood in the context of anxiety or fear; however, many subjects, following exposure to a particularly stressful event, also manifest anhedonia, dysphoria, externalized anger and increased aggression or dissociative symptoms. The diverse range of symptoms reported depends on various factors, including genetic/temperamental predisposition and learned coping patterns to stress.

5.4.1 ADJUSTMENT DISORDERS

Adjustment disorders are characterized by depressive symptoms, anxiety and/or behavioural changes, without fully satisfying the criteria for a proper depressive or anxiety disorder, following an event experienced as stressful and with marked difficulty in implementing an adaptive response to the increased demand for cognitive and emotional resources as coping with such stressor would require.

Any life event can be stressful, and the ability to cope with such events varies between different individuals, so there is no defined list of stressors. To cite a few examples, there may be marriage or divorce, relocation, financial difficulties, health problems.

Epidemiology and course

The prevalence of Adjustment Disorders in outpatient psychiatric populations, depending on the studies and the sample, varies between 5% and 20%, reaching peaks of 50% in psychiatric inpatients.

ADs are ubiquitous and can appear at any age, with concerns of differential diagnosis in children and adolescents, as clinical presentation in these populations is very similar to neurodevelopmental disorders.

Risk factors

- personality disorders
- cognitive disturbances
- substance abuse

Comorbidity

Theoretically, an AD can occur in any subject regardless of its already known psychiatric or physical medical diagnosis, with which they are often associated. ADs are associated with high suicidal risk and a high rate of successful suicides. The AD can have an acute course if it lasts less than 6 months or persistent/chronic if it lasts more than 6 months (in the persistence of the triggering factor and in any case no later than 6 months from the interruption of the trigger).

Clinical presentation

The characteristic element of AD is the identification of an external and stressful life event after which the disorder occurs. AD usually begins within 3 months of the onset of the stressor and generally lasts up to 6 months after the end of the stressor itself. The triggering life event can be of various types, it can be single (e.g. parenthood, relationship interruption) or multiple (e.g. work, marital and health difficulties), repeated (e.g. frequent moving, work) or continuous (e.g. chronic illness). The subjective discomfort is manifested with loss of function in work/school settings and difficulties in social relations. It can also complicate the course of the underlying medical condition (e.g. noncompliance to check-ups or medical therapies). The AD may primarily present with a low mood, with anxiety, with anxious-depressive symptoms, with alterations in emotion and behaviour (e.g. disorganized behaviour, self-harm, substance abuse for self-medication purposes).

DSM-5 Diagnostic Criteria:

A. The development of emotional or behavioural symptoms in response to an identifiable stressor (s) occurring within 3 months of the onset of the stressor (s).

B. These symptoms or behaviours are clinically significant, as evidenced by one or both of the following:

1. Marked distress that is out of proportion to the severity or intensity of the stressor, taking into account the external context and the cultural factors that might influence symptom severity and presentation.

2. Significant impairment in social, occupational, or other important areas of functioning.

C. The stress-related disturbance does not meet the criteria for another mental disorder and is not merely an exacerbation of a pre-existing mental disorder.

D. The symptoms do not represent normal bereavement.

E. Once the stressor or its consequences have terminated, the symptoms do not persist for more than an additional 6 months.

Treatment

The first treatment choice in AD is psychotherapy, with various approaches (e.g. group therapy, individual psychotherapy). The aim is to provide the patient with new strategies for managing stressful events, improving and strengthening individual resources and with a focus also on the prevention of future episodes.

Pharmacotherapy aims to reduce symptoms. Depending on the current distress, drugs of choice are anxiolytics (e.g. mid half-life benzodiazepines, administered for a limited period in order to reduce tolerance and dependence) and/or antidepressants (the most tolerable are SSRIs, but SNRIs and TCAs can be used too).

5.4.2 POST-TRAUMATIC STRESS DISORDER (PTSD)

Definition

Post-Traumatic Stress Disorder (PTSD) is a disease that can occur in people who have suffered or witnessed a traumatic or violent event, or if a traumatic experience happened to a loved one.

The experience of a traumatic event of various kinds (e.g. wars, robberies, child abuse, muggings, kidnapping, terroristic attack, torture, natural disasters or due to the action of man, serious car accidents…), determines the onset, at variable times (in the first weeks or after several months), of a symptomatology, that includes emotional and cognitive symptoms, and neuro-vegetative alterations. Characteristic is re-experiencing the traumatic event in a recurring, involuntary and intrusive way detail of the traumatic event, whose memories are very vivid and are associated with sensory, emotional, physical and behavioural components. Therefore, the clinical presentation of PTSD is very variable: in some subjects the dysphoric component prevails, in others, the fear of reliving the trauma becomes central, in still others dissociative symptoms prevail.

Epidemiology

The incidence of PTSD is about 8-15% in the general population, with some geographic differences (e.g. higher prevalence in the United States than in Europe, Asia, Africa), according to other meta-analyses and statistics on adult subjects the global annual prevalence is 1-6%. In North America (namely USA and Canada), lifetime prevalence rates are higher (6.1-9.2%) than in other high- and middle-income countries (2.3%) according to WHO data.

The difference in prevalence between sexes (10% females versus 4% males) could be explained by the greater global spread of sexual assaults and rapes against females, which are far more common in all societies, rather than wars and physical violence for men.

Up to 30-50% of people who have suffered violence, genocide, war veterans but also medical providers, police officers and firefighters, develop symptoms that lead to the diagnosis of PTSD.

Prognosis

Symptoms can have a fluctuating course, with exacerbations during periods of greater stress. Without treatment, about half of the patients achieved remission of symptoms after one year.

Positive prognostic factors are the rapid onset, duration less than 6 months, good previous functioning, good social support, absence of other comorbidities.

The course of the disease is typically chronic: only ⅓ of the patients recover within a year, while another ⅓ remain symptomatic even 10 years after the traumatic event. The presence of PTSD is associated with numerous consequences, e.g. employment difficulties, less insertion and social support, difficulties in interpersonal relationships and affections, a greater degree of disability, increased risk of death from other causes (e.g. cardiovascular disease, diabetes) but also suicide (suicide attempts and actual deaths from suicide, in particular in the case of past childhood abuse).

Comorbidity

In adults, comorbidity is common with:

- depression
- bipolar disorder
- anxiety disorder

- substance abuse
- conduct disorder
- physical illnesses, e.g. autoimmune, endocrine, pulmonary, dementia, high cardiovascular risk, dementia

In children, comorbidity is more common with:

- separation anxiety disorder
- oppositional defiant disorder
- major neurocognitive disorder

Aetiopathogenesis

The factors that contribute to the development of the disorder are:

- Stressor: a stressor alone is not sufficient but is necessary to cause the disorder. Except for factors relatively common to daily life, however stressful (e.g. bereavement, illness, divorce), possible triggering stressors are very varied, and not only the experience itself but also the emotional/cultural connotation that the subject associates with it are important;
- Individual risk factors: since not all traumatic experiences generate PTSD in all subjects, risk factors have been studied that increase the likelihood that a person will develop PTSD at the same stressor:
    - Physical or sexual abuse in childhood
    - Female gender
    - Youthful age
    - Repeated exposure to traumatic events
    - Objective severity of the event or degree of direct exposure
    - personality disorder
    - Belonging to ethnic minorities, low socioeconomic status, poor psychosocial resources
    - Being a widower, separated, divorced
    - History of psychiatric disorders or positive psychiatric family history
    - excessive use of alcohol recently

Aetiologic hypotheses have been proposed for the development of PTSD:

- Psychoanalytic model: the trauma brings a quiescent but unresolved psychological conflict to light, determining in the subject a state of repression, denial, immobility.
- Cognitive-behavioural model: the subject is unable to rationalize the trauma and for this reason, they relive it continuously, implementing avoidance behaviours to the factors that reactivate the memory itself. There are two distinct phases in this model:
    - in the first phase, the trauma (unconditioned stimulus) produces a fear that is elicited by specific stimuli (physical or mental, such as sight, sounds, smells) causing conditioning;
    - In the second phase, the repetition of the conditioned stimulus evokes the fear response, even in the absence of the original unconditional stimulus (the trauma). To avoid this state of malaise, the subject takes avoidances concerning both the unconditioned stimulus and the conditioned stimuli/stimuli associated with it. Furthermore, the potential secondary advantage of this condition should not be underestimated, typically assuming a condition of protection, compassion and care by third parties;

- biological basis: the paradigm of “learned behaviour” has highlighted the role of various neurotransmitters and somatic systems in the onset of PTSD symptoms:
    - noradrenergic;
    - dopaminergic;
    - GABAergic;
    - endogenous opioids: a low concentration of plasma β-endorphins and an analgesic response to opioid antagonists (e.g. naltrexone) have been observed in veterans with PTSD;
    - hypothalamic-pituitary-adrenal axis: low levels of plasma and urinary cortisol, increased glucocorticoid receptors in lymphocytes and poor ACTH response after CRF stimulation have been observed in subjects with PTSD; cortisol hyper-suppression could predict those subjects who will develop the disorder and those who will not, given the exposure to same traumatic events; the hyper-activation of this axis though differs from other mental disorders;
    - autonomic nervous system: an increase in orthosympathic tone leads to an increase in heart rate and blood pressure, tremors, sweating and palpitations, sleep disturbance (fragmentation and increased sleep latency); desensitization of the α2- and β-adrenergic receptors was observed and as per chronic down-regulation; at the level of laboratory tests, increased concentrations of urinary catecholamines are observed.

Clinical presentation

After the traumatic event, acute stress-induced disturbances may develop with dissociative characteristics (e.g. derealization, depersonalization) and sleep disturbances. During the first month of these symptoms, the diagnosis of Acute Stress Disorder is initially made, and only if symptoms last over a month the diagnosis of PTSD can be formulated (criterion F). Such symptoms tend to disappear after a few months, in cases with a favourable prognosis (about 1/3 of cases), thanks to the activation of resilience and stress management mechanisms. On the contrary, when the prognosis is less favourable (1/3 of cases), the course can be chronic (3-6 months after the trauma) with a progressive structuring of the psychopathological picture. There are also late-onset forms, which develop at least 6 months after the event and are a slight harder to properly recognize.

The characteristic symptoms can be grouped into four clusters: intrusive symptoms, avoidance, cognitive and mood changes, arousal and hypervigilance.

- Intrusive symptoms occur independently of the patient's will and are characterized by recurrent and intrusive unpleasant memories or dreams of the event, the sensation of reliving the experience, with illusions, hallucinations and flashbacks. The individual may act or feel as if the event was recurring if exposed to factors that recall the event (conditioned stimulus), and intense mental and physical discomfort follow. The subject may experience feelings of shame, guilt, anger, sadness, vulnerability, fear/terror with sense of unreality (“like in a dream”), strangeness (“like in a movie”), perception of one's body as different, abnormal or extraneous, confusion, absence of space-time references. To these elements is added a set of autonomic symptoms, analogous to the acute anxiety crisis or panic attack, which consists of profuse sweating, dyspnoea, sudden crying, tachycardia, nausea, diarrhoea, tremors, hypervigilance and cognitive activation.
- The great malaise that follows the re-enactment leads patients to avoid all conditioned stimuli (e.g. thoughts, sensations, conversations, activities, places or people) that evoke the trauma.

- A peculiar aspect of PTSD is psychogenic amnesia: it is real lacunar amnesia relating to the traumatic event, different from the more frequent dissociative amnesia, in which the subject has a distorted memory of the trauma, with an inability to recall the timeline or details. There is also psychic numbing, affective flattening, apathy and anhedonia. Affectivity is reduced, with feelings of diminishing future prospects. The loss of future prospects, the freezing in a hopeless present, the so-called “guilt of the survivor”, the negative vision of the world, the feeling of indelible change and the irreversibility of what was before are typical symptoms of the pathological reaction to exposure to an extreme event. Cognitive and mood alteration, as well as intrusive symptoms, can lead to self-injury and impulsive behaviour, socio-occupational impairment, alcohol, or substance abuse. The maladaptive aspects resulting from the disorder present a particular gender difference: in women, they mainly concern self-care, while for men they concern the intake of alcohol and drugs, unregulated behaviour and an increase in suicidal attempts.
- Another typical symptom is hyperarousal (state of hyper activation) which is characterized by:
  - Difficulty falling asleep or staying asleep
  - Irritability or outbursts of anger
  - Difficulty concentrating
  - Hypervigilance (feeling of "tense nerves", inability to "let your guard down")
  - Exaggerated alarm responses (sudden jerks for minimal stimuli)

The diagnosis of PTSD requires the presence of a series of psychic and autonomic symptoms, but there are also "sub-threshold" forms (especially in the elderly, as stated above) in which not all symptoms are present but where the post-traumatic nature of the disorder is the same. Despite the syndromic incompleteness, these forms have a suicide risk equal to the full expression forms.

Clinical presentation changes depending on the traumatic stimulus and the age of the subject:

- children change their behaviour and mood, reduce social interactions, decrease school performance;
- In adolescents, violent behaviours prevail, with a high risk to health; they lose ambition, become irritable and aggressive;
- In adults, the disorder manifests as hyperarousal, avoidance, sleep problems, worsening health, and suicidal ideation.

DSM-5 diagnostic criteria:

A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:

1. Directly experiencing the traumatic event(s).

2. Witnessing, in person, the event(s) as it occurred to others.

3. Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.

4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains: police officers repeatedly exposed to details of child abuse).

B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:

1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).

2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s).

3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.)

4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).

5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).

C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:

1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).

2. Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).

D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:

1. Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs).

2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., “I am bad,” “No one can be trusted,” ‘The world is completely dangerous,” “My whole nervous system is permanently ruined”).

3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others.

4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, or shame).

5. Markedly diminished interest or participation in significant activities.

6. Feelings of detachment or estrangement from others.

7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).

E. Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:

1. Irritable behaviour and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects.
2. Reckless or self-destructive behaviour.
3. Hypervigilance.
4. Exaggerated startle response.
5. Problems with concentration.
6. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).

F. Duration of the disturbance (Criteria B, C, D, and E) is more than 1 month.

Treatment

The most effective treatment for PTSD seems to be the combination of drugs (that treat comorbidities) and psychotherapy (that treat the typical symptoms of the disorder).

SSRIs (e.g. sertraline, paroxetine) and SNRIs are currently the first lines of treatment, reducing the symptomatology with good tolerability and safety profile. It is also possible to use TCAs (e.g. imipramine, amitriptyline) using dosages equivalent to those of depressive disorder (range 50-100 mg per day), and continuing the treatment for at least one year. Other drugs that can be used are MAOIs, mood stabilizers (e.g. carbamazepine, valproate) and trazodone. Benzodiazepines are also used, albeit with caution given the frequent comorbidity with alcohol and substance abuse.

To regulate sleep at night, hypnotics and sedatives can be used. Adjunctive preventive interventions can be the administration of α1-antagonists in the evening to reduce the occurrence of nightmares and the administration of β-blockers in response to the hyperactivity of the noradrenergic system.

Antipsychotics (e.g. haloperidol) are reserved for the management of major agitation.

Psychotherapy must help the patient cope with the rejection of trauma, eliminate the source of stress, metabolize all the emotions associated with the event and restore the correct sleep-wake rhythm. As a psychotherapeutic approach, one can opt for both psychodynamic therapy and cognitive-behavioural therapy. Two different cognitive-behavioural modalities can be used: one involves the use of both gradual and implosive/intense exposures and can be performed in vivo or through images or films; the other provides the patient with tools to manage anxiety and stress through cognitive and/or relaxation techniques so that they can be “skilled” when a trigger or conditioned stimulus occurs during the day.

A relatively recent psychotherapeutic technique is Eye Movement Desensitization and Reprocessing (EMDR): during sessions, a sensory "bilateral stimulation" (auditory, ocular, tactile) is performed while the patient evokes the traumatic event. This technique allows the patient to activate the brain system responsible for processing the traumatic memory in order to make the associated emotions conscious and integrate them with the other information available. The subject then through a “catharsis”, in a state of deep relaxation, relives and removes the traumatic event without being overwhelmed. Finally, Mindfulness has found good efficacy in reducing post-traumatic symptoms.

5.4.3 DISSOCIATIVE DISORDERS

Definition

In this type of disorder, the various systems that underlie complex mental activity (consciousness, memory, identity, emotions and perception), which are normally experienced as a continuum and in constant integration with each other, lose mutual integration. Disconnection between the various systems can produce positive or negative symptoms. The term "positive" indicates something more than the normal state of consciousness: unwanted intrusions into consciousness and behaviour, with loss of the continuity of subjective experience. On the contrary, the term "negative" indicates something less than the usual experience: the individual is unable to access information or control mental functions that are generally easily accessible or controllable.

BOX: THE CASE OF ANNA O.

Anna O. (literary name for Bertha Pappenheim) was a 21-year-old girl with numerous qualities and talents, from a good Austrian family, who found herself having to take care of her seriously ill father neglecting her diet and physical health.

In the winter of 1880, a few months after her father's illness, she began to develop varied and changing symptoms physically, neurologically and psychically, which could not be explained by the medical knowledge of the time. Symptoms included convergent strabismus, paralysis of the right upper limb and then of the two lower limbs, hydrophobia, alterations in the state of consciousness with estrangement from conversations during which she rehearsed events in her imaginative "private theatre", splitting of personality, sudden mood swings, complex hallucinations, mutism.

Admitted at the Salpêtrière hospital, she was treated by Joseph Breuer, who was a luminary in hypnosis and in the treatment of hysteria. Breuer decided to apply hypnosis to "make the patient speak" when she became completely silent: she was able to overcome the speech block, and even the muscular paresis gradually resolved. However, the patient's clinical presentation fluctuated and then worsened after the death of her father. Sigmund Freud also worked at the Salpêtrière hospital and discussed the case with Breuer: they decided to try a new type of therapy, called the "cathartic method", which was making the patient speak freely about everything that went through the mind. When Anna O told a memory surfaced in her mind, the related symptom disappeared, as if she was able to give "free rein" to unpleasant and burdensome emotional contents hidden from consciousness. Thanks to this speech therapy in 1882, Anna was finally free of symptoms.

Dissociative disorders in DSM-5 include:

- dissociative identity disorder
- dissociative amnesia
- depersonalization/derealization disorder

DISSOCIATIVE IDENTITY DISORDER

We speak of dissociative identity disorder (formerly referred to as "multiple personality disorder") when there are two or more distinct personality states (as in Dr Jekyll and Mr Hyde) or an experience of possession: these people do not decide to behave in one way or another, they do not act consciously, because there is a sharp discontinuity in the sense of self and awareness of their actions without the patient exercising their will. Dissociative identity disorder is a failure of identity integration: each of the personality states can be experienced as if it had a personal history, self-image and distinct identity, including a separate name.

Epidemiology

The disorder has a prevalence of 1.4% in females and 1.6% in males; no prevalence studies are available in individual states.

The onset can take place at any age. In children, there are mainly problems with memory, concentration and attachment, in adolescence, it presents with sudden changes in identity; in adults, they may resemble a late onset of mood disorders, OCD, cognitive disorders due to dissociative amnesia.

Risk factors

It is often found in association with overwhelming experiences, traumatic events, chronic childhood trauma, physical or sexual abuse in childhood (in general 70-100% of cases, compared to 8-17% in the general population in the US).

Comorbidity

DDI is often comorbid with other psychiatric pathologies, although the assessment can be sometimes difficult in some studies the main comorbidities are:

- PTSD (79-100%)
- Borderline personality disorder (31-83%)
- Avoidant personality disorder (76%)
- Substance abuse (83-96%)
- Depression (83-96%)
- somatoform disorder

In such patients, the suicidal risk is very high: over 70% of outpatient patients attempt suicide and multiple attempts are frequent as well as self-harming behaviours.

The functional consequences of the disorder can have varying degrees of impairment (from minimal to profound), occur more frequently in a relational than professional context, and a tendency to minimize the impact of symptoms is common.

Clinical presentation

There is usually a primary identity that bears the official name of the subject, and which is usually passive, dependent, tending to feelings of guilt and depression; the other identities frequently have different names and characteristics that conflict with the primary identity: e.g., they are extremely irritable or hostile, "executive", and aggressive towards others or self-destructive.

There are also important memory alterations: frequent memory gaps about their personal history, both remote and recent. Amnesia is frequently asymmetric through the identities: more passive identities tend to have poorer memories, while more hostile, "executive", or "protective" ones have more complete memories; an identity that does not have control functions may however have access to consciousness through the production of auditory or visual hallucinations (e.g. a voice giving instructions). The demonstration of amnesia can be achieved by witnesses or through the "discoveries" of the individual himself (e.g. the fact of finding at home items of clothing that the subject does not remember having bought).

The symptoms produced by the disintegration of identity are:

- Feeling depersonalized observers of their own speeches and actions
- Perception of voices
- Strong emotions and egodistonic and disconcerting impulses
- Sudden changes in attitudes, perspectives and personal preferences
- Perception of one's body as different
- Non-epileptic seizures or other conversive symptoms
- Dissociative amnesia has the following characteristics:
- Gaps in the remote memory of personal life events
- Memory errors related to acquired procedures
- Discovery of evidence of daily actions and tasks that he does not remember having performed
- Dissociative fugues are common in these patients.

<u>DSM-5 diagnostic criteria:</u>

A. Disruption of identity characterized by two or more distinct personality states, which may be described in some cultures as an experience of possession. The disruption in identity involves marked discontinuity in sense of self and sense of agency, accompanied by related alterations in affect, behaviour, consciousness, memory, perception, cognition, and/or sensory-motor functioning. These signs and symptoms may be observed by others or reported by the individual
B. Recurrent gaps in the recall of everyday events, important personal information, and/or traumatic events that are inconsistent with ordinary forgetting.
C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The disturbance is not a normal part of a broadly accepted cultural or religious practice.
   Note: In children, the symptoms are not better explained by imaginary playmates or other fantasy play.
E. The symptoms are not attributable to the physiological effects of a substance (eg, blackouts or chaotic behaviour during alcohol intoxication) or another medical condition (eg, complex partial seizures).

Differential diagnosis

- Alcohol or benzodiazepine intoxication (they can both produce amnesia, which is usually anterograde and generalized), cannabis, hallucinogens, ketamine, ecstasy (they can cause depersonalization symptoms).

- General medical conditions, e.g. dementia (it is characterized by retrograde amnesia, with progressive loss of memory, usually starting from recent events with preservation of autobiographical information), epilepsy (it causes limited amnesia of the moments during and shortly after a crisis). In particular, in the case of dissociative amnesia, the patient will have a good performance on neuropsychological tests, showing particular deficits in autobiographical information, in contrast to dementia patients.

- PTSD: it is characterized by symptoms of re-experiencing, avoidance, hypervigilance and arousal.

- Borderline Personality Disorder, where the fragmentation of identity is only slightly less than in the DID.

- Schizophrenia and other psychotic disorders where hallucinations occur: in the case of DDI, auditory hallucinations and other psychotic symptoms are “customed” on the identity of who is in charge at the moment, and they are more often pseudo-hallucinations (the patient feels them from the inside). The occurrence of auditory hallucinations in patients with DID is already reported from childhood, then it becomes more fluctuating and independent of the other symptoms.

- Bipolar disorder: in DID the fluctuations of emotional states are very rapid, even in a few hours, and abrupt, often in response to environmental stimuli; in contrast, mood swings in bipolar disorder last at least 2 weeks (for major depressive episode) or 4-7 days (for hypo-manic episodes) and their occurrence and recovery is independent of external circumstances.

- Factitious disorder and simulation: the patient deliberately produces physical or mental symptoms to obtain attention and play the role of the sick person, or to obtain a particular secondary advantage such as a disability pension or avoid certain types of duties. The symptoms are presented "from the textbook" in a very simple way, without complex pictures or the distress and shame that patients with DID feel, insight and judgment are perfectly preserved, unlike DID.

Treatment

Psychotherapeutic approach is fundamental, and involves the combination of various techniques (psychoanalysis, cognitive and behavioural therapy, hypnosis, family therapy) in addition to drug treatment.

Drug therapy aims to reduce secondary depressive symptoms and stabilize mood. Symptoms attributable to the sphere of traumatic disorders (intrusive thoughts, hyper-excitability and hypervigilance) are partially responsive to drugs.

Eye Movement Desensitization and Reprocessing (EMDR) therapy has been indicated in PTSD in recent years, some case reports suggest that it can be extended to dissociative disorders, but no systematic studies have been conducted.

Among the drugs that can be used are SSRIs, TCAs and MAOIs, β-blockers, clonidine, anticonvulsants, and benzodiazepines. In some individuals with a tendency to irritability and

aggression, carbamazepine can be used; atypical antipsychotics (risperidone, quetiapine, ziprasidone, olanzapine) are preferable to first-generation antipsychotics in the control of anxious and intrusive symptoms.

DISSOCIATIVE AMNESIA

It is a disorder characterized by the inability to remember autobiographical information, usually limited to a traumatic event, which should be kept in memory and which are usually easily accessible.

A subtype of dissociative amnesia is a dissociative fugue, which manifests as sudden travel or wandering accompanied by anterograde amnesia for this event.

Epidemiology and course

It has a prevalence of 1% in males and 2.6% in females (in a US sample); the lifetime prevalence is around 6-7% (based on a Canadian and a Turkish sample).

The onset can be sudden in generalized amnesia, less evident in the limited forms and can arise at any age (small children, adolescents, adults).

The natural course of the disease provides that the occurrence of a first episode predisposes to the recurrence of subsequent episodes. The duration of the single episode can vary from minutes to decades and after remission, intense discomfort, suicidal behaviour, PTSD symptoms may remain. Suicidal risk is high: suicidal and self-destructive behaviours are common, particularly after sudden remission with the onset of intolerable memories.

Comorbidity

The disorder can present comorbidities of the dissociative, trauma-related area, depression, substance abuse and personality disorders, significantly worsening the prognosis of patients.

Clinical presentation

The types of amnesia that can occur are:

- Limited amnesia: limited to a limited period
- Selective amnesia: only about some events of a limited period
- Generalized amnesia: total memory loss of one's personal history (rare), personal identity, previous knowledge of the world (semantic knowledge) and already known skills (procedural knowledge); has an acute onset with perplexity and disorientation
- Systematized amnesia: related to a specific category of memories

The person with dissociative amnesia cannot recall both episodic and semantic memories from the autobiographical memory; on the opposite, the ability to store new information, cognitive functions, procedural memory and language are preserved. The distinction between accessible memories and those that cannot be recalled is typically sharp, unlike the normal functioning of memory (we normally remember recent events more easily and boundaries between different memory domains are softer).

The functional consequences are a varying degree of impairment, from limited to severe.

Although there are few systematized studies on this condition, it seems that the severity of the disorder and amnesia for very early events are correlated with a longer duration and severity of the trauma, typically childhood.

DSM-5 diagnostic criteria:

A. An inability to recall important autobiographical information, usually of a traumatic or stressful nature, that is inconsistent with ordinary forgetting.
   Note: Dissociative amnesia most often consists of localized or selective amnesia for a specific event or events, or generalized amnesia for identity and life history.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
C. The disturbance is not attributable to the physiological effects of a substance (eg, alcohol or other drug of abuse, a medication) or a neurological or other medical condition (eg, partial complex seizures, transient global amnesia, sequelae of a closed head injury/traumatic brain injury, other neurological condition).
D. The disturbance is not better explained by dissociative identity disorder, posttraumatic stress disorder, acute stress disorder, somatic symptom disorder, or major or mild neurocognitive disorder.

Differential diagnosis

- normal forgetfulness of autobiographical memory
- cognitive impairment
- PTSD and acute stress disorder
- other dissociative disorders
- substance abuse
- head trauma
- fictitious disorder/simulation

Treatment

The treatment of dissociative amnesia involves primarily a cognitive psychotherapeutic approach. Pharmacological treatment protocols have not been standardized. In cases of acute onset, in a hospital setting, benzodiazepines or barbiturates can be used to "facilitate" the patient's access to information, which can then be consciously processed.

DEPERSONALIZATION/DEREALZATION DISORDER

Definition

- Depersonalization is a psychopathological condition in which the individual feels detached from themselves, from aspects of their own self (feelings, thoughts, body or parts of his body, sensations), or divided (out-of-body experience).
- Derealization is defined as a state in which the individual can feel as if they were in the fog, in a dream, in a bubble, as if there was a veil or a glass wall between themselves and the world.

Depersonalization and derealization are frequent symptoms in psychiatric care settings as they might be present almost in all other mental conditions (see "differential diagnosis"), and they are not diagnostic per se. In fact, we might say that the diagnosis of a "pure" depersonalization/derealization disorder is a diagnosis of exclusion, once we have ruled out all other possible mental (and organic) disorders.

Epidemiology and course

A large part of the population experiences these symptoms at least once in their life, without distinction of gender: depending on the studies and the sample, they range from 12% up to about 50%.

The prevalence of depersonalization/derealization disorder, on the other hand, is just 0.8-2.8% in the general population. The onset occurs on average in adolescence; it can be sudden or gradual. The duration of the single episode can vary from hours to years, there can be a persistent course characterized by separate or continuous episodes, the intensity of which can be variable or stable.

Risk factors

- acute trauma
- other psychiatric disorders, e.g. anxiety disorders or depression
- substance abuse
- childhood trauma
- the sudden death of a loved one
- growing up with a parent with severe psychiatric illness
- disturbances or doubts about sexual orientation

Comorbidity

- major depressive disorder
- anxiety disorders
- obsessive-compulsive disorder
- avoidant personality disorder
- borderline personality disorder

Aetiology

The cause of this disorder is not fully known, but several hypotheses have been formulated:

- Psychodynamic: depersonalization is a defence reaction of the ego in situations of disintegration of the self (e.g. extreme-pain, trauma).
- Traumatic stress: Up to 60% of people with life-threatening experiences report at least one transient episode of derealization during the traumatic experience or immediately after.

- Neurobiological theory: the association between depersonalization and migraine and the use of cannabis, the positive response to SSRIs and the increase in personalization symptoms in conditions of tryptophan depletion indicate an involvement of the serotoninergic system. Through pharmacological elicitation studies of dissociative states, it seems that the glutamatergic system, through the NDMA receptor, is central to the origin of symptoms.

Clinical presentation

Symptoms of depersonalization are abnormal body experiences, emotional or physical blunting, temporal distortion with abnormal subjective memories.

Symptoms of derealization are subjective visual distortions (blurring, amplified acuity, widening or narrowing of the visual field, macropsia or micropsia) and auditory distortions (amplified or muted voices and sounds). The functional consequences for the subject are represented by the fact that the symptoms can be very distressing and associated with severe morbidity; they can involve relational and professional impairment due to hypo-emotion towards others or a sense of disconnection from everyday life.

DSM-5 Diagnostic Criteria:

A. The presence of persistent or recurrent experiences of depersonalization, derealization, or both:
    1. **Depersonalization** – Experiences of unreality, detachment, or being an outside observer with respect to one's thoughts, feelings, sensations, body, or actions (eg, perceptual alterations, distorted sense of time, unreal or absent self, emotional and/or physical numbing).
    2. **Derealization** – Experiences of unreality or detachment with respect to surroundings (eg, individuals or objects are experienced as unreal, dreamlike, foggy, lifeless, or visually distorted).
B. During the depersonalization or derealization experiences, reality testing remains intact.
C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The disturbance is not attributable to the physiological effects of a substance (eg, a drug of abuse, medication) or another medical condition (eg, seizures).
E. The disturbance is not better explained by another mental disorder such as schizophrenia, panic disorder, major depressive disorder, acute stress disorder, posttraumatic stress disorder, or another dissociative disorder.

Differential diagnosis

Depersonalization/derealisation can be a symptom in the context of other mental disorders:

- schizophrenia
- panic disorder
- acute stress disorder
- PTSD
- other dissociative disorders
- borderline personality disorder
- avoidant personality disorder

- substance abuse (e.g. cannabis, hallucinogens, ketamine)

It can also be present in other types of disorders of organic origin:

- temporal lobe epilepsy
- vestibular disorders
- sleep apnoea
- head injuries or infections (e.g. Lyme disease) or autoimmune disease with central involvement

Treatment

In the absence of psychiatric comorbidities, the first-line treatment for DDD is psychotherapy, which can have a cognitive-behavioural approach, but also psychodynamic, hypnotherapeutic and supportive approach. However, there is a lack of placebo-controlled studies or comparisons between the various options, so the choice will fall on availability in the treatment centre and the patient's desire. Patients can also try stress management techniques, active distraction, reduction of sensory stimulation, relaxation, physical exercise.

As drug therapy in patients who also have an anxiety or depressive disorder, the first drug choice falls on SSRIs (but also TCAs, mood stabilizers, typical and atypical antipsychotics), while benzodiazepines can be used in the short term to control anxiety symptoms.

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