Mohamed Kheider University Of Biskra

Faculty of Human and Social Sciences

Department Of Psychology & Educational Sciences

Adult & Geriatric Psychopathology

Lectures intended for first-year master's students in clinical psychology

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General Introduction

General Introduction

Psychopathology, or the study of mental disorders, is a multifaceted field that requires a comprehensive understanding of abnormal behaviors. It focuses on the study of the symptoms and underlying causes of psychological disorders. The traditional etymological structure of "psychopathology" offers an intriguing first sense of the word: psyche pathos ology the mind's suffering under study conditions.(Mansager & Garrison, 2022, p. 1).It is a broad academic field that examines people's experiences, thoughts, feelings, and emotions in non-typical forms, as well as their personalities and groups. First and foremost, it is crucial to recognize that this important branch of psychology is connected to broader clinical fields such as psychiatry, psychiatric nursing, social work, and medical sciences in general. In addition, it serves many essential functions in psychology and related fields.

According to Mansager and Garrison (2022), the core functions of psychopathology vary in the literature, but generally include at least four propositions for the main goals of psychopathology: (1) it is descriptive, in that it attends to the phenomenological experience of the person suffering psychopathology; (2) it is clinical in its linking the phenomenological with the classification (nosology) of psychopathologic experience; (3) it is theoretical by stipulating the foundational causes (etiology) of the psychopathologic experience; and (4) it is structural in its efforts to expose the meaningful coherence of psychopathologic experience.

As people age, psychopathology can manifest differently, with the elderly being more susceptible to cognitive disorders and mental health issues. This complexity requires clinical psychologists to understand and evaluate the elements contributing to both mental and physical illnesses.

The Adult and Geriatric Psychopathology module at Masters level aims to identify common mental health disorders during this period of life, explore their clinical signs

and features, causes and effects, and focus on the clinical application of this knowledge. The courses focus on the in-depth study of mental disorders, covering their theoretical foundations, causes, development, symptoms and diagnosis, providing students with the essential skills to understand and differentiate a range of disorders.

Teaching Module: Adult & Geriatric Psychopathology

Coefficient : 2

Credits: 05

Weekly Hours: 1h30

Assessment Method: Continuous assessment + exam

General Objectives: Learners will be capable of:

- Develop a fundamental understanding of various disorders.
- Identify the key characteristics of these conditions.
- Describe the typical presentation of patients with any problem or condition.
- Determine the etiology of the different disorders.
- Develop a differential diagnosis for these disorders based on clinical and anamnestic information.

Unit 1: Anxiety Disorders

Anxiety Disorders

Objectives

- Describe the principle features of anxiety disorders.
- Gain a deeper understanding of anxiety disorders.
- Understanding the factors underlying these disorders.
- Identify the major biological systems involved in the disorders.
- Distinguish different anxiety disorders from other psychiatric or medical disorders.

Introduction

Anxiety disorders, a widespread group of mental health conditions, are marked by intense and persistent feelings of fear, tension, and worry. These disorders are notably more severe and long-lasting than the typical anxiety people experience in response to everyday challenges. The DSM-5 identifies several specific types of anxiety disorders, such as generalized anxiety disorder, panic disorder, and phobic disorders. These conditions share common symptoms that affect physiological, cognitive, and behavioral aspects, often leading to considerable emotional distress and hindering daily functioning.

1 Definition

In DSM-5,anxiety (French: anxiété; German:Angst) is defined as the anticipation of future threat; it is distinguished from fear (peur; Furcht), the emotional response to real

or perceived imminent threat. Further, the term worry (souci; Sorge) in DSM-5 adds an additional nuance by referring to the cognitive aspects of apprehensive expectation. Anxiety is a normal emotion. From an evolutionary viewpoint, it is adaptive since it promotes survival by inciting persons to steer clear of perilous places. Since the 20th century, anxiety has also been a disorder in psychiatric classifications. The clinical threshold between normal adaptive anxiety in everyday life and distressing pathological anxiety requiring treatment is subject to clinical judgment. (Crocq, 2015).

According to Weems & Silverman (2013) anxiety is the product of a multicomplex response system, involving affective, behavioral, physiological, and cognitive components . Worry, for example, is one component of anxiety that can be viewed as a cognitive process preparing the individual to anticipate future danger. Fear, in contrast, is part of the response system that fosters preparation for either freezing to avoid impending punishment or escaping as part of the fight/flight response.

2 Historical Context

According to Crocq (2015), the first signs of interest in anxiety go back far into philosophical and medical history.In Greek philosophy, phobia was introduced as a medical disorder through the case of Nicanor, a case mentioned in the Hippocratic Corpus (460-370 BC); whose fear of flute music at night illustrates a persistent pathological fear.Additionally,Cicero's Tusculan Disputes and other Latin Stoic writings classify anxiety (angor) as a disease (aegritudo), separating it from melancholia and defining its clinical features, including ruminative worry and constriction. Cicero prefigured contemporary ideas of "state" worry and "trait" worry.

From a philosophical perspective, the Stoic and Epicurean schools of thought of Seneca (On the Peace of Mind) and Lucretius (De Natura Rerum) respectively promoted mental peace by emphasizing the present, reducing the fear of death, and curbing

excessive cravings. These methods are in line with modern mindfulness practices and cognitive treatments. By combining philosophical and medical ideas that are relevant to contemporary methods, ancient philosophers established fundamental viewpoints on recognizing and treating anxiety.

The word anxiety derives from the Latin substantive angor and the corresponding verb ango (to constrict). A cognate word is angustus (narrow). These words derive from an Indo-European root that has produced Angst in modern German (and related words in Dutch, Danish, Norwegian, and Swedish). Interestingly, the same relationship between the idea of narrowness and anxiety is attested in Biblical Hebrew. In fact, Job expresses his anguish literally with the Hebrew expression "the narrowness (tsar) of my spirit.

In French, as well as in other Romance languages,anxiété (anxiety; from the Latin anxi$^{\smile}$etas) is often differentiated from angoisse (anguish; from the Latin ang$^{\smile}$ust$^{\smile}$ıa). Sometimes, the two terms are considered synonymous by some authors. More frequently, a nuance is established: anxiety designates a psychological feeling whereas anguish designates the somatic experience.

Joseph Lévy-Valensi (1879 to 1943), defined "anxiété" " as a dark and distressing feeling of expectation. Anxiété was described as including the psychological and cognitive aspects of worrying. In contrast, "angoisse" was defined as the experience of spastic constriction of voluntary or involuntary muscle fibers. Angoisse (anguish) could be experienced as a constriction affecting the muscles of all systems; kaleidoscopic manifestations were mentioned in Lévy-Valensi's book: bronchial spasm, shortness of breath, intestinal cramps, vaginismus, urinary urgency, pseudo–angina pectoris, headache. In other Romance languages, as in French, anxiety and anguish may be considered more or less synonymous by some authors; if other authors do find a nuance, anxiety then bears the connotation of psychological worry whereas anguish implies a somatic feeling of constriction. A look at the reference dictionaries of various Romance languages

confirms that the same nuance of meaning is reproduced in the word pairs ansiedad vs angustia in Spanish, ansietat vs angoixa in Catalan, ànsia or ansietà vs angòscia in Italian, and ansiedade vs angústia in Portuguese.The only exception is the most eastern Romance language, Romanian. Anxietate, the word used in Romanian medical articles to translate anxiety,seems to be a recent loanword from the French anxiété,first attested to in 1934. One of the traditional Romanian words for anxiety is neliniște (unrest), a negation of liniște (quiet, rest), from the Latin lenis (smooth, mild).

The concept of anxiety as a distinct illness seems to have disappeared from historical documentation during the period between classical antiquity and the emergence of modern psychiatry. Although individuals experienced anxiety, it was classified under different terms. Among these alternative diagnoses, Beard's neurasthenia became the most prominent and influential.

The Anatomy of Melancholy, a comprehensive analysis of the literature from antiquity to the 17th century, was published in 1621 by Robert Burton. According to Allan W. Horwitz, Burton's writings are frequently cited in relation to depression. But anxiousness was another issue for Burton. The definition of melancholia at the time included anxiety as well as depression. In general, a range of clinical images exhibiting negative affect or internalizing symptoms might be used to diagnose melancholia. The ability to maintain silence was a crucial component of melancholia; a patient who was disturbed met the criteria for a diagnosis of mania, or furor in Latin. For Burton, grief and terror were closely related.

The first major French medical nosology was established by Boissier de Sauvages (1706–1767), who bridged classical antiquity and modern science through Sydenham's clinical methodsBoissier's taxonomy included 10 disease classes and 2,400 species (individual diseases). Mental disorders, termed 'vesaniae,' were part of the 8th class and divided into four orders :

- **Hallucinations**, comprising Vertigo, Suffusion, Diplopia, Syrigmus (ie, imagi-

nary noise perceived in the ear), Hypochondriasis, and Somnambulism;

- **Morositates**, including Pica, Bulimia, Polydipsia, Antipathia, Nostalgia, Panophobia (ie, panic terror), Satyriasis, Nymphomania, Tarantism (ie, immoderate craving for dance), and Hydrophobia ;

- **Deliria** comprising Paraphrosine (ie, temporary delirium caused by a substance or a medical illness), Amentia (“universal” delirium without furor); Melancholia (“partial” and non-aggressive delirium with sadness and chronicity), Mania (“universal delirium”with furor and chronicity), Demonomania (ie, melancholia attributed to the devil)

- **Folies** anomales comprising Amnesia, and Agrypnia (ie, insomnia).

In the late 19th and early 20th centuries, anxiety became central to emerging diagnostic categories like neurasthenia and neuroses. George Miller Beard introduced neurasthenia in 1869, describing a range of symptoms, including anxiety and chronic depression. Sigmund Freud distinguished anxiety neurosis from neurasthenia and introduced enduring terminology for anxiety disorders. Pierre Janet, a contemporary of Freud, developed the concept of "psychasthenia," linking anxiety to subconscious fixed ideas. Despite evolving perspectives, neurasthenia persisted into modern classifications like the ICD-10.

Emil Kraepelin focused on anxiety as a symptom of other illnesses rather than addressing it as a separate condition. In his ninth edition, he described anxiety as the most common negative affect that affects the body and the mind, and he connected inner tension to anhedonia. He mixed obsessive-compulsive thinking with phobias, even though he acknowledged that phobias had their own category. Furthermore, by highlighting the role anxiety plays in manic-depressive illness, Kraepelin’s work foreshadowed the DSM-5’s "anxious distress" specifier for bipolar disorder. He pointed out that severe restlessness, hopelessness, or self-destructive activities might result from anxiety in manic-depressive patients, linking excessive anxiety to a higher chance of suicide.

DSM-5 introduced a number of substantial and clinically relevant changes in the classification of anxiety and related disorders. One of the most striking was the decision to have separate chapters for anxiety disorders, obsessive-compulsive and related disorders, and trauma- and stressor-related disorders. This decision reflects the growing evidence base on the diagnostic validity and clinical utility of these different groupings. Furthermore, adoption of these new groupings helps to explain a number of other changes in DSM-5, including some of the new diagnostic criteria. (Stein et al., 2014)
The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM5) lists separation anxiety, selective mutism, specific phobia, social anxiety disorder (also called social phobia), panic disorder, agoraphobia, generalized anxiety, substance abuse/medication-induced anxiety, and anxiety disorder caused by another medical condition in its chapter on anxiety disorders.(Kehoe, ,2017,p.7)

3 Clinical features

A core defining feature of anxiety is emotion dysregulation of the anxiety response system . Such dysregulation may involve intense and disabling worry that does not help anticipate true future danger, or intense fear reactions in the absence of true threat. Distress/impairment may also result from dysregulation in corresponding negative emotional states (e.g., being upset or overconcerned). For convenience we refer to these primary features of anxiety problems as anxious emotion. These core features of anxiety may be expressed behaviorally (e.g., avoidance), cognitively (e.g., concentration difficulties), physiologically (e.g., dizziness, racing heart), or interpersonally (e.g., difficulty making friends). These features cut across all of the anxiety disorders in the DSM-IV. In contrast, secondary features of anxiety are aspects that differentiate specific categories of anxiety disorder . For example, worry about separation from parents is specific to separation anxiety disorder, being embarrassed in public is specific to so-

cial anxiety disorder, and uncued panic attacks are specific to panic disorder.(Weems & Silverman, 2013, pp. 513–514) In these lectures, we will focus on three disorders: generalized anxiety, panic disorder and phobic disorder.

Generalized Anxiety Disorder (GAD)

1 Definition

Generalized Anxiety Disorder (GAD), as described in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), is characterized by persistent and excessive worry that persists for at least six months on most days, leading to considerable distress or disruption in daily functioning. Clinically, GAD typically involves heightened anxiety over seemingly minor matters, frequently accompanied by physical symptoms and unhealthy behavioral changes.

The worry is impairing across varied contexts (e.g., work, home, and social). Symptoms which are required for diagnosis include feeling restless, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, and sleep disturbance.(Patriquin and Mathew,2017,p2) Most studies suggest a peak onset of GAD during late adolescence or early adulthood, but it can also present later in life.(DeGeorge et al., 2022)

2 Clinical features of Generalized Anxiety Disorder

The main clinical characteristics according to DSM 5 include anxious anticipation and difficulty managing anxiety. Additional symptoms may include an inability to handle situations and memory loss.

GAD people contain a broad range of features and varying degrees of severity. Some patients can place more emphasis on a particular symptom than others that are often related to GAD's highly enhanced physiological arousal, emotional lability and muscular stress, fatigue, restlessness, and difficulty sleeping. Some other symptoms seen in a person suffering from GAD include an excessive attachment to any unnecessary thing, un-

necessary emphasis on something, lack of concentration, weakening of memory, rapid heartbeat, and inability to remain stable and calm. Also, symptoms like physical weakness, irritability, restlessness, etc. are included.(Mishra et al.,2023,p4)

3 Aetiology

Several factors that can contribute to the development and persistence of Generalized Anxiety Disorder (GAD) were summarized in Llera and Newman (2015), including genetic, interpersonal, environmental, cognitive, emotional, and neurobiological elements. Twin and family studies suggest a genetic predisposition to GAD, as evidenced by higher concordance rates among monozygotic twins compared to dizygotic twins and a tendency for those with GAD to have first-degree relatives also afflicted by the disorder. The personality trait of neuroticism, which is both highly heritable and linked to GAD, explains a significant part of the genetic variance in GAD.

Environmentally, individuals with GAD often report negative, uncontrollable experiences in their past and problematic early relationships with caregivers. These issues may lead to ongoing difficulties in personal relationships, such as marital dissatisfaction and hypersensitivity to social threats. Cognitively, people with GAD exhibit heightened awareness of threats, interpret neutral situations as threatening, and have inflexible thinking patterns, which may contribute to excessive worrying, particularly about relationships.

Emotionally, those with GAD experience more intense emotions and struggle to recover from negative states. Physiologically, they display lower heart rate variability and higher sympathetic activity, indicating elevated emotional arousal. Neurologically, individuals with GAD show increased activity and structural differences in areas of the brain associated with fear and anxiety, such as the amygdala and the dorsomedial prefrontal cortex, enhancing their reactivity to negative stimuli.

Neuropsychologically, Anxiety disorders, including generalized anxiety disorder (GAD), are associated with cognitive impairments in attention, working memory, and executive functions. Research shows that anxiety related to the anticipation of an electric shock can impair working memory, but has a minimal effect on planning. Different anxiety disorders may affect cognition differently, suggesting a distinction between beneficial and detrimental anxiety. Functional neuroimaging studies reveal that people with GAD have increased activity in the amygdala and insula, areas linked to the processing of negative emotions. This suggests shared neural mechanisms underlying various anxiety disorders, including GAD.

GAD is believed to be caused by dysregulation in the body's fear-response systems, which are primarily located in the amygdala and hippocampus. Changes in the function of these regions can result in heightened fear and anxiety responses. Brain imaging studies using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have revealed structural and functional abnormalities in patients with GAD. For example, increased activity was observed in the amygdala and insula, which are involved in processing emotions and interpreting physical sensations. Additionally, people with GAD have decreased connectivity between the prefrontal cortex and amygdala, which is thought to help regulate emotional responses.

Moreover, neurotransmitter imbalances, such as serotonin, dopamine, and gamma-aminobutyric acid (GABA), can contribute to GAD. GABA, the principal inhibitory neurotransmitter in the brain, reduces neuronal excitability and promotes calm and relaxation. People with GAD frequently have decreased GABA levels, increasing anxiety and fear responses.

At the physiological level, individuals with Generalized Anxiety Disorder (GAD) often display more baseline physiological dysregulation than those without GAD or with other anxiety disorders. They usually have lower heart rate variability, higher heart rates, and increased skin conductance. However, this hyperarousal is not always con-

sistent and can change based on the context. For instance, those who worry a lot show increased sympathetic nervous system activity and decreased HRV. Worrying beforehand can reduce cardiovascular reactivity to fearful imagery, while relaxation or neutral stimuli before such exposure can heighten it. This suggests that people with GAD experience chronic physiological arousal and heightened cardiovascular reactivity in anxiety-provoking situations. Additionally, they exhibit elevated startle responses at baseline, indicating persistent anxious thoughts even without immediate threats. Therefore, GAD is marked by a distinct psychophysiological profile of increased baseline arousal and heightened reactivity to threats.
(for more see Gkintoni, E., & Suárez Ortiz, P., 2023; Patriquin, J. & Mathew, J., 2017; Stein, M. B., & Steckler, T., 2010)

4 Theoretical models of generalized anxiety disorder

4.1 Avoidance model of worry (AMW) and GAD

The Avoidance Model of Worry and GAD (AMW; Borkovec, 1994; Borkovec et al., 2004) is based on Mowrer's (1947)two-stage theory of fear, and also draws from Foa and Kozak's emotional processing model . The AMW asserts that worry is a verbal linguistic, thought- based activity that inhibits vivid mental imagery and associated somatic and emotional activation. This inhibition of somatic and emotional experience precludes the emotional processing of fear that is theoretically needed for successful habituation and extinction.

On the other hand, enhancement of somatic and emotional experience can lead to effective processing of emotional cues. Habituation and extinction are made possible through exposure to the entire spectrum of fear cues, including the feared stimulus itself, the response to the stimulus, as well as the potential meaning behind the fear . Therefore, worry can be seen as an ineffective cognitive attempt to problem solve and

thus remove a perceived threat, while simultaneously avoiding the aversive somatic and emotional experiences that would naturally occur during the process of fear confrontation . Furthermore, the experience of worry becomes negatively reinforced. According to the AMW, catastrophic mental images that make their way into the worry process are replaced by less distressing, less somatically activating verbal linguistic activity. Thus, worry is negatively reinforced by the removal of aversive and fearful images . In addition, worry is further reinforced by positive beliefs, such as a belief that worry is helpful for problem-solving, motivating performance, and avoiding future negative outcomes. Positive beliefs are reinforced when negative future events do not occur or are effectively managed, thus further reinforcing the worry.(Behar et al.,2009,p.p 1012-1013)

4.2 The intolerance of uncertainty model (IUM)

Intolerance of Uncertainty (IU) is a difficulty in managing negative emotions due to unclear or insufficient information and the perception of uncertainty. Generally it's seen as "an underlying fear of the unknown ». The Laval research team introduced IU in the early 1990s while studying generalized anxiety disorder (GAD). The Intolerance of Uncertainty Model of GAD (IUM) proposed by Dugas et al. in 1998 identifies four factors that contribute to worry in GAD: Intolerance of Uncertainty (IU), Positive Beliefs about Worry (PBW), Negative Problem Orientation (NPO), and Cognitive Avoidance (CA). The concept was originally developed by the Laval team working on models and treatments of generalized anxiety disorder (GAD) in the early nineties.

Bottesi et al. (2016) describe Intolerance of Uncertainty (IU) as the challenge individuals face in handling negative emotions due to ambiguous or incomplete information and the perception of uncertainty. Those with high IU find uncertain situations threatening, distressing, and undesirable, regardless of the actual likelihood of a negative outcome. The Intolerance of Uncertainty Model of GAD (IUM), proposed by Dugas et al. in 1998, outlines four factors that contribute to the onset and maintenance of worry in

GAD: IU, Positive Beliefs about Worry (PBW), Negative Problem Orientation (NPO), and Cognitive Avoidance (CA).

Extensive research has shown that Intolerance of Uncertainty (IU) is a key cognitive vulnerability factor for worry and a sustaining factor for generalized anxiety disorder (GAD).Negative beliefs about uncertainty hinder an individual's ability to effectively handle uncertain situations, leading them to use worry as an ineffective coping mechanism to prevent feared outcomes. Positive Beliefs about Worry (PBW) involve distorted views about the benefits of worry; these beliefs often create false contingencies that serve as both positive (e.g., the belief that worrying can yield effective solutions) and negative (e.g., the non-occurrence of feared events) reinforcements, thereby maintaining the habit of worrying. Individuals with Positive Beliefs about worry see worry as a positive trait, thinking that "being a worrier means being thoughtful," and believe that it is an effective strategy for problem-solving, preventing negative situations, avoiding unpleasant emotions associated with negative events, and motivating action.

Negative Problem Orientation (NPO) is characterized by a pessimistic outlook on problems, accompanied by a set of negative cognitive and emotional reactions triggered by problem situations. It is linked with low confidence in one's problem-solving abilities, a perceived lack of personal control over the problem-solving process, and a pessimistic view of problem-solving outcomes. People with GAD often do not employ problem-solving strategies effectively and do not view themselves as capable problem solvers, even if they possess adequate problem-solving knowledge.

Cognitive Avoidance (CA) involves mental strategies to avoid or suppress unwanted thoughts, particularly fearful mental images that trigger physiological responses. CA includes various techniques (both automatic and controlled) such as replacing threatening thoughts with neutral or positive ones, converting mental images into verbal-linguistic thoughts, and more. This process is particularly significant in the context of GAD.

4.3 The metacognitive model (MCM)

The metacognitive model of GAD (Wells, 2010) highlights the basic psychological factors and processes that are thought to underlie most types of disorders, as illustrated in the figure 1.1

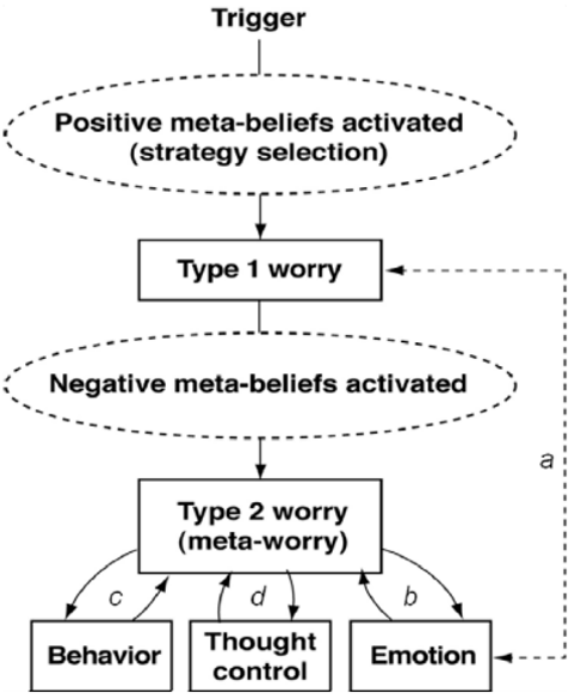


Figure 1.1. The metacognitive model of GAD
Adapted from Wells (2010, p. 134).

Theoretical expositions of the development and maintenance of worry are generally couched within the context of excessive worry and its role in generalized anxiety disorder (GAD). Wells and colleagues (Wells, 1995, 2006; Wells & Carter, 1999; Wells & Matthews, 1994) emphasize the role that processes such as metacognitive beliefs, metacognitive appraisals, and thought control strategies play in the maintenance of excessive and uncontrollable worry in their metacognitive model (MCM) of GAD (Wells, 1995).

According to the MCM, threat-related triggers activate positive metacognitive beliefs about worry as an effective means of coping with the events represented in these intrusive images and thoughts. These beliefs emphasize the perceived benefits of worry as a means of ensuring that one will be able to cope with a feared outcome, be adequately prepared for a worst-case scenario, or that worry helps to ward off disaster . When confronted by threat, individuals who hold positive beliefs about worry will thus be inclined to initiate chains of intrusive catastrophizing ('what if?') questions in an attempt to generate ways of coping with threat-related triggers . This process underpins what is known as Type 1 worry .

Generally, anxiety dissipates once an individual perceives themselves to have generated sufficient options for dealing with the threat they are confronted with and can thus disengage from the worry process. This, in turn, serves to reinforce positive beliefs about worry as an effective coping strategy. In contrast to positive beliefs about worry, negative beliefs about worry revolve around themes of worry as uncontrollable and potentially dangerous. The activation of negative beliefs about worry results in negative appraisals of worry, which Wells (2006) refers to as Type 2 worry or meta-worry. Type 2 worry generally leads to an increase in threat appraisal and thus an intensification of anxiety. Type 2 worry serves to prolong episodes of worry by interfering with internal signals to disengage from the worry process. This process is primarily facilitated via a range of avoidant behaviours and thought control strategies . The result is a continuation of the worry cycle, resulting in the excessive worry that characterizes GAD.(Pretorius et al.,2015,p. 235)

According to Adrian Wells(2010) The metacognitive model identifies several feedback loops that maintain Generalized Anxiety Disorder (GAD), illustrated previously in Figure 1.1:

- **Type 1 Worry**: This involves initial worry about potential dangers, which increases anxiety. However, once the individual appraises that the worry has helped in coping or avoiding danger, anxiety may decrease. This fluctuation in anxiety levels can reinforce the utility of worry, influencing whether thinking needs to be sustained or reduced.

- **Type 2 Worry**: Anxiety symptoms themselves can exacerbate worries about worrying (meta-worry), where symptoms are seen as indicators of mental or physical harm. This escalates the perceived threat, potentially leading to greater anxiety and even panic attacks.

- **Avoidance Behaviors**: Actions like avoiding anxiety-inducing situations, using substances like alcohol, or seeking reassurance hinder the individual's realization that they can control their worry and that it is benign. This perpetuates the negative beliefs about worry.

- **Thought Suppression**: Attempts to suppress worrying thoughts often lead to their paradoxical intensification (thought rebound), failing to alleviate worry. This ineffective strategy supports ongoing negative beliefs about the uncontrollability of worry. Even when suppression works temporarily, it can prevent the individual from learning that worry is non-threatening, thus sustaining fears about the dangers of worrying.

These loops highlight how GAD is sustained by a combination of ineffective coping strategies and reinforcing negative beliefs about worry and its control.

4.4 The emotion dysregulation model(EDM)

The Emotion Dysregulation Model (EDM) draws from the literature on emotion theory and the regulation of emotional states in general .The EDM also shares features with Linehan's conceptualization of emotional deficits in borderline personality disorder . The EDM consists of four central components .The first component asserts that individuals with GAD experience emotional hyperarousal, or emotions that are more intense than those of most other people. This applies to both positive and negative, but particularly to negative, emotional states. Second, individuals with GAD have a poorer understanding of their emotions than do most individuals. Third, they have more negative attitudes about emotions (e.g., the perception that emotions are threatening) than do others. Finally, they evidence maladaptive emotion regulation and management strategies that potentially leave them in emotional states that are even worse than those they initially set out to regulate.

Each of the four EDM components has several tenets. For instance, subsumed under the first component of the model (intensity of emotions) are the assumptions that individuals with GAD have a lower threshold for the experience of emotion than do others, and that emotions occur more easily and quickly, rather than just more strongly, among individuals with GAD. Moreover, perhaps due to the hypothesized greater intensity of and lower threshold for emotions, individuals with GAD are also expected to express emotions more frequently than others, and this is particularly the case for negative emotions.

The second component (poor understanding of emotions) subsumes deficits in describing and labeling emotions, as well as in accessing and applying the useful information that emotions convey. The combination of components 1 and 2 is hypothesized to lead to the third component, which stipulates that individuals with GAD become overwhelmed, anxious, or uncomfortable when strong emotions occur, thereby creating a

feedback loop. Individuals with GAD are also hypothesized to show extreme hypervigilance for threatening information and increased attention either toward or away from emotions and pertinent negative beliefs. Finally, this sequence culminates in the fourth component, which specifies that individuals with GAD make unsuccessful or maladaptive attempts to either minimize emotions or over-control emotions, or inappropriately express emotional arousal (e.g., excessive worry, suppression of emotions, emotional outbursts). As such, worry plays a fundamental role in this model as an ineffective strategy to cope with emotions. According to Mennin and colleagues, however, this succession of events can also proceed in the opposite direction (i.e., maladaptive emotion regulation strategies leading to increased negative emotion), thereby giving rise to a bidirectional cycle of emotion dysregulation and negative affect.(Behar et al.,2009,p.p 1017-1018)

4.5 The Acceptance-Based Model (ABM) of GAD

This model emphasizes an individual's tendency to narrow her/his focus toward threatening or future oriented information, to respond negatively, to attempt and to avoid her/his internal experiences (such as anxious thoughts and emotions), and to avoid or restrict her/his engagement in important areas of her/his life. Thus, one core area of difficulty is a problematic relationship with internal experiences, characterized by distress, judgment, fusion and reactivity, which intensifies emotional responding . This in turn leads to chronic, rigid attempts to control and avoid internal experiences, which further increases distress and impairs quality of life , while also increasing reactivity to one's internal experiences. For example, research and theory suggest that worry is a form of cognitive avoidance that may interfere with successful emotional processing , and that attempts to rigidly control one's internal experiences often paradoxically amplify distress .

These patterns of avoidance often extend to other areas of an individual's life as well. It is not uncommon for individuals with GAD to restrict their participation in meaningful activities (e.g., interpersonal relationships, employment opportunities) in an attempt to avoid unwanted negative internal experiences . When they do engage in these activities, individuals with GAD often report not being fully "present" as their focus on worry and future oriented threat occupies their attention .(Treanor et al.,2011,p.2)

The ABM involves four components: (a) internal experiences, (b) a problematic relationship with internal experiences, (c) experiential avoidance, and (d) behavioral restriction.As mentioned in (E. Behar et al,2009), The model suggests that difficulties in managing internal experiences (such as thoughts, feelings, or bodily sensations) involve two main issues: (1) negative responses to internal experiences, and (2) fusion with these experiences. The first issue, negative responses to internal experiences, encompasses negative thoughts (for instance, judging emotional responses as too intense or unwelcome) or meta-emotions (like the fear of feeling fear). Such reactions complicate the individual's ability to monitor, accept, and understand their emotions. This issue shares conceptual similarities with the Emotion Dysregulation Model's focus on negative perceptions of emotions (such as viewing emotions as threatening; Mennin et al., 2002). The second issue, fusion with internal experiences, refers to becoming deeply intertwined with these negative responses, leading to a belief that these fleeting negative reactions are enduring traits of the individual.

The third component of the model, experiential avoidance, involves actively or passively avoiding internal experiences deemed threatening or negative, such as excessive worrying about future events or minor issues to avoid deeper concerns. The final component, behavioral restriction, refers to the diminished participation in meaningful activities, like spending time with family, which often results from increased experiential avoidance.

This avoidance can extend to other valuable activities, potentially reducing presence and awareness in those moments. Over time, this behavioral restriction reinforces itself, as individuals with Generalized Anxiety Disorder (GAD) engage less in or are less aware during meaningful activities, leading to heightened distress and perpetuating a cycle of negative internal experiences and further avoidance.

5 Diagnosis

Diagnosis of GAD can be made by using the DSM-5 diagnostic criteria. The criteria are correlated to the patient's social life and the consequent effects.
SM-5 criteria for general anxiety disorder: GAD is diagnosed by excessive and extreme anxiety occurring for the past six months for most of the days. The uncontrollable anxiety may interrupt with patient's social life (such as school, occupation). A person can be diagnosed as suffering from GAD if three or more of the following symptoms are presented:

- Restlessness.
- Easy fatiguability.
- Concentration issues or mind going blank.
- Irritability.
- Tension of muscles.
- Sleep disturbance.

When diagnosing GAD, the following points should also be taken care of:

- Sleep disturbance should not be caused by physiological effects of a substance or medical conditions.

- The patient should not be affected by other mental disorders such as panic disorder, OCD, Depression.
- Anxiety should cause remarkable distress or impairment in patients.

ICD-11: Essential diagnostic criteria for GAD set by the WHO (World Health Organization) are called ICD-11 (international classification of diseases, 11th revision). It describes GAD as "anxiety that is generalized nonstop, but not because of any environmental conditions (e.g., substance use disorders)", mainly focusing on physiological stimulation (such as sweating and palpation). Symptoms may vary, but include persistent nervousness, tension of muscles, sweating, palpitation, dizziness, and epigastric discomfort. (Bamalan et al., 2023, p. 42)

6 Psychotherapies for patients with GAD

The table 1.1 provides a detailed overview of various psychotherapeutic approaches for managing Generalized Anxiety Disorder (GAD), as identified by Jeremy DeMartini et al. in 2019. Each therapy is outlined with key notes on its execution and underlying principles, offering insights into how these therapies address the complex symptoms of GAD.

Table 1.1. Psychotherapies for Patients With GAD.

Type of Therapy	**Notes**
Cognitive behavioral therapy	This therapy is traditionally delivered in 12 sessions and focuses on examining and changing unhelpful thoughts and behaviors that perpetuate anxiety. Elements of cognitive behavioral therapy may also be learned with minimal therapist involvement or through self-help tools (using books, audio/video, the Internet, and smartphone apps), although many have not been rigorously tested. Techniques include education, exposure therapy, relaxation training and biofeedback, and problem-solving techniques.
Supportive psychotherapy	A commonly practiced and nondirective form of therapy that focuses on supporting the patient's self-esteem. In a warm and nonjudgmental environment, the therapist carefully listens to the patient and provides reassurance and encouragement.
Psychodynamic therapy	An insight-oriented form of therapy that aims to resolve unconscious conflicts that are believed to result from early-life relationships. Techniques include clarifications, interpretations, and confrontations.
Mindfulness	A type of meditation in which patients learn to increase awareness of the present. Patients are encouraged to focus on bodily sensations, emotions, and thoughts in a nonjudgmental manner.
Acceptance and commitment therapy	This therapy shares similarities with mindfulness and cognitive behavioral therapy. Patients learn to focus on the present and accept thoughts or practice strategies to distance themselves from internal thoughts and sensations, a technique called cognitive defusion.

(Jeremy DeMartini et al.,2019)

Panic disorder

1 Definition

Panic disorder (PD) is an anxiety disorder characterized by spontaneous and recurrent panic attacks (PAs) which is severe and persistent, as specified by The Diagnostic and Statistical Manual of Mental Disorders 5th ed. (DSM-5). The key event in panic disorder is the panic attack, which is an abrupt surge of intense fear or discomfort that is diagnostically characterized by a cluster of 13 physical and cognitive symptoms, including palpitations, shortness of breath, parasthesias, trembling, derealization, and fears of dying, going crazy, or losing control (American Psychiatric Association , 1994)
According to Clark (1986) “the panic attack consists of an intense feeling of apprehension or impending doom which is of sudden onset and which is associated with a wide range of distressing physical sensations. These sensations include breathlessness, palpitations, chest pain, choking, dizziness, tingling in the hands and feet, hot and cold flushes, sweating, faintness, trembling and feelings of unreality”.(Fava & Morton,2009,p.624)

It should be noted that while panic attacks are a defining feature of panic disorder, they may occur as symptoms of phobic disorders as well, in which case they are precipitated by the feared stimulus. Panic attacks may also occur sporadically in the absence of an anxiety disorder.(Smoller et al.,2008,p.118)

2 Brief history

Panic disorder was first regarded as a diagnostic entity with the publication of the DSM III, 25 years ago. Prior to that time, panic attacks were viewed as symptoms of a general neurosis, although accounts of a clinically similar syndrome appeared much earlier.

These were labeled as soldiers heart , neurocirculatory asthenia , and effort syndrome . In the DSM-III, agoraphobia was considered a separate disorder, which might or might not be associated with panic attacks. Observations of clinical samples by Klein (1981) and others suggested that agoraphobia generally developed following panic attacks, and this led to a redefinition of agoraphobia as a secondary response to panic attacks in the DSM-III-R . However, the debate continues , and the DSM-IV-TR (1994) retains agoraphobia without a history of Panic Disorder as a separate diagnosis.

In contrast to earlier DSM diagnostic criteria, greater recognition is given in DSM-IV to the notion that panic attacks may occur in the context of any anxiety disorder. Panic attacks are categorized as either situationally bound, situationally predisposed, or unexpected/uncued. Panic Disorder is diagnosed when there are repeated unexpected/uncued panic attacks and persistent apprehension about panic attacks and/or behavioral changes resultant from panic attacks.(Arch & Craske, 2008, p.5). The DSM-5 classifies Panic Disorder under the category of Anxiety Disorders .

3 Description of symptoms and criteria

Panic attacks are characterized by a unique action tendency: Specifically, urges to escape, and less often, urges to fight. In other words, panic attacks represent activation of the fight-flight system. Accordingly, panic attacks usually involve elevated autonomic nervous system arousal, needed to support such fightflight reactivity. Furthermore, perceptions of imminent threat, such as death, loss of control, or social ridicule frequently accompany the fight-flight responsee. However, the urgency to escape, autonomic arousal, and perception of threat are not present in every self-reported occurrence of panic. For example, data gathered from ambulatory (portable) devices have found sympathetic nervous system activation although nonactivation has also been documented (for 40% of self-reported panic attacks). Severe panic attacks are more auto-

nomically based . Self-reported panic in the absence of actual autonomic activation is assumed to reflect anticipatory anxiety versus true panic . Another discordant example occurs when perceptions of threat or danger are refuted, despite the report of intense fear and arousal. This has been termed noncognitive panic .

Panic attacks may be experienced by individuals diagnosed with any of the anxiety disorders, and they are common in all of these disorders. Panic disorder is distinguished by unexpected panic attacks, or attacks that occur without an obvious trigger, and at least 1 month of persistent apprehension about the recurrence of panic or its consequences, or a significant behavioral change. These behavioral changes may include safety behaviors, such as frequent attendance at medical facilities for fear of a medical problem, or agoraphobia. Agoraphobia refers to avoidance, or endurance with dread, of situations from which escape might be difficult or in which help might be unavailable in the event of a panic attack, or paniclike symptoms, such as loss of bowel control. Typical agoraphobic situations include shopping malls, waiting in line, movie theaters, traveling by car or bus, crowded restaurants and stores, and being alone. A subset of individuals who have panic disorder also experience nocturnal panic attacks. Nocturnal panic refers to waking from sleep in a state of panic with symptoms that are very similar to panic attacks that occur during wakeful states . Nocturnal panic does not refer to waking from sleep and panicking after a lapse of waking time, or night-time arousals induced by nightmares or environmental stimuli (such as unexpected noises). Also, nocturnal panic is distinct from sleep terrors and sleep apnea . Individuals who suffer frequent nocturnal panics often become fearful of sleep and attempt to delay sleep onset. Avoidance of sleep may result in chronic sleep deprivation, in turn precipitating more nocturnal panics.(Arch & Craske, 2008, p.p2-3)

4 Panic disorder subtypes

PD is a variable disorder in terms of physical, physiological and cognitive symptoms of panic attack. It has been suggested that, since there are panic attacks consisting of very different symptom clusters, there may be subtypes of this disorder and that failure to distinguish these subtypes may lead to theoretical, methodical and treatment errors . For these reasons, subtyping studies based on factor analysis of symptoms during panic attacks have been conducted . Several features have been taken into account in order to detect subtypes of PD. Presence of agoraphobia, nocturnal panic attacks, prominent symptoms during panic attacks, timing of panic attacks, biological features of the disorder, genetic liability are among these features. PD has been subtyped into different groups, regarding prominent panic attack symptoms as PD with heart and pulmonary symptoms , vestibular symptoms, gastrointestinal symptoms , depersonalization/derealization or without subjective sense of fear.(Konkan et al.,2013,p.334)

5 Aetiology

5.1 Biological theories

5.1.1 Genetic Theories

Johannes Schumacher et al(2011) identified several genetic markers significantly associated with an increased risk of panic disorder, emphasizing the importance of neurotransmitter systems, particularly serotonin and norepinephrine pathways. Specific single nucleotide polymorphisms (SNPs) in genes such as COMT, MAOA, and ADORA2A were highlighted as potential contributors to the genetic susceptibility to panic disorder. These findings suggest that disruptions in these neurotransmitter systems play a critical role in the pathophysiology of panic disorder. The study underscores the rele-

vance of genetic factors in the development of panic disorder and suggests that further research into these genetic associations could enhance diagnostic accuracy and lead to more targeted treatments for individuals affected by this condition.

5.1.2 Neurobiolgical theory

Several neurobiological theories have been proposed to explain the pathogenesis of panic disorder. Gorman et al. has suggested a neuroanatomic model that integrates the different views of panic disorder as either biological or a psychological disease. According to Gorman's model, fearful responses and panic attacks are mediated by a "fear network" in the brain that is centered in the amygdala and interacts with the hippocampus and medial prefrontal cortex. This neuroanatomical model has stimulated additional research, primarily in neuroimaging studies. In this special issue, Lai(2018) has pursued an additional theoretical approach using the traditional fear network model of panic disorder and has highlighted an extended and advanced fear network model of panic disorder. In the advanced fear network model, sensory regions of the temporal-parietal-occipital lobe have critical roles in the development of fear and anxiety. In addition, the insular integrates filtered sensory information via the thalamus from the sensory regions of the occipital, parietal, and temporal lobes and sends the information to the frontal regions for cognitive processing, and to the limbic system for primitive response, which causes the imbalance in panic disorder.(Kim,2019,p.1)

5.1.3 Hormone Theory

According to Karpinski et al. (2017), elevated plasma oxytocin levels have been reported in patients with OCD, suggesting a potential neuroregulatory role of oxytocin in OCD. Oxytocin may also be involved in OCD pathology through its effects on other neurotransmitter systems. A study by Yoshida et al. suggested that oxytocin increases the release of serotonin, which may contribute to its role in OCD.

5.1.4 Respiratory theories

Increased CO2 sensitivity hypothesis suggests that panic attacks may originate in the brain stem. The first line of evidence points to symptoms caused by autonomic nervous system impulses. The second relates to CO2-induced panic attacks, which affect the brain stem's respiratory centers. Klein's hypothesis proposes that panic attacks result from a malfunction in an evolved alarm system that monitors suffocation signals, activated by metabolic signs of asphyxia. However, no specific "false suffocation alarm" system has been identified anatomically or functionally. Studies on CO2 sensitivity have shown mixed results due to confounding variables and individual differences. Additionally, several brain stem nuclei, including the nucleus tractus solitarius, locus coeruleus, and raphe nuclei, are implicated in panic responses and may serve as suffocation detectors. Panic disorder patients also seem to lose some homeostatic control after respiratory stress.

Another assumption of CO2 sensitivity had been proposed by Genetic predisposition hypothesis , suggesting genetics influence CO2-induced panic, with CO2 sensitivity possibly being a familial trait marker and a phenotypic expression of genetic predisposition preceding panic disorder. Genetic mechanisms may involve chemoreceptor expression and neurotransmitter system impacts, with potential for identifying genetic markers to prevent panic disorder. However, it is unclear if CO2 sensitivity and hyperventilation are common to all individuals or specific to those with panic disorder. CO2 sensitivity might be linked to a panic disorder subtype, a hypersensitive homeostatic response ("false suffocation alarm"), or nonspecific receptor irritation.(for more, see Sardinha et al., 2009)

5.2 Cognitive theories

Clark's theory of misinterpretations suggests that panic disorder results from catastrophic misinterpretation of benign bodily sensations of unclear or ambiguous origin, and that educating patients to interpret their bodily sensations realistically is an effective therapeutic intervention.(Rofé and Rofé,2015,p.44)

This earlier cognitive theory by Clark supposed that development and maintenance of PD is proposed to begin from the first Panic Attack, which most often occurs during a time of stress and is accompanied by "catastrophic misinterpretations" of somatic and other sensations as key. Irrespective of the source of an individual's internal physical sensations, an individual could develop panic, which in turn leads to catastrophic thoughts about their impending doom, such as "I am going to die", or "I am having a heart attack". The catastrophic thoughts sustain the vicious cycle, where anxiety provoking thoughts produce further somatic symptoms and continues the cycle of catastrophic thinking, thus inevitably ends in a PA. Internal focus on somatic and physical sensations has been linked to persistent vigilance and hypersensitivity to normal and common symptoms .

An element of self-efficacy was added into the vicious cycle where it is argued that an individual's negative perception of their coping abilities against threat also acts as a perpetuating factor to PA . The self-efficacy was perceived as parallel yet simultaneous in sustaining the vicious cycle. According to this particular cognitive model, one's low self-esteem results in high arousal which begins the panic cycle. Cognitive and personality factors have been implicated.(Kyriakoulis & Kyrios, 2023, p.5).

There has been controversy in the literature about the relationship between agoraphobia and panic disorder. The prevailing view in American psychiatry, as reflected in DSM-IV, has been that agoraphobia (AG) is almost always a complication of panic disorder (PD).An alternative view, more closely allied with European psychiatry and re-

flected in ICD-10, is that agoraphobia is a distinct disorder which may or may not follow the onset of panic attacks. In ICD-10,the diagnosis of panic disorder with agoraphobia is given only if a primary diagnosis of agoraphobia has been excluded. Epidemiologic studies support the notion that AG can commonly occur in the absence of panic disorder. In the National Comorbidity Survey Replication study, approximately 40% of individuals with AG never met criteria for PD (Smoller et al.,2008,p.119)

Phobic disorder

1 Definition

Phobias are a type of anxiety disorder characterized by an extreme, irrational fear of particular objects, situations, or activities that are typically safe or only marginally threatening. This overwhelming fear can seriously interfere with a person's daily functioning, often triggering extreme anxiety, panic attacks, and avoidance behaviors. Unlike ordinary anxiety, which can be more scattered and less concentrated, phobias are extremely concentrated and provoke a powerful emotional reaction to the fear-provoking stimuli, causing people to take considerable measures to avoid it.(Muhammad Akram et al,2024,p.1)

A phobia is a persistent and disproportionate fear of a specific object or situation that presents little or no actual danger to a person" (Carson et al., 2003). DSM-5 has divided phobic disorders into three categories of phobias: specific phobia, social phobia and agoraphobia.

- **Specific Phobia** has five subtypes: animals (e.g., snakes, spiders, dogs); natural environment (e.g., water, heights, storms); blood-injection-injury; situational (bridges, tunnels); others (vomiting, choking, 'space phobia' where the person has a fear of falling down if he/she is away from walls or support).

- **Social Phobia** is a fear of social situations. A person is afraid of acting in a humiliating or embarrassing way when he/she is exposed to the scrutiny of others. Social phobia may be specific to a situation such as fear of public speaking or generalised as in fear of many different social interactions.

- **Agoraphobia** is a fear of crowded places such as shopping malls, theaters etc. It can also be a fear of having a panic attack in situations where escape might prove

to be difficult or embarrassing

2 History of phobic disorders

Historically, extreme fears of specific situations or objects have been documented as far back as the ancient Greeks and Romans. In the late 19th and early 20th centuries, Sigmund Freud proposed that phobias were a psychological defense mechanism arising from repressed psychological conflict. These ideas influenced early psychological thought on phobias but were later critiqued and expanded upon.In the early 20th century, behaviorism became a dominant force in psychology—researchers like John B. Watson and B.F. Skinner emphasized observable behaviors and learning through conditioning. Phobias were often seen as learned responses, with specific phobias thought to develop through classical conditioning (associating a neutral stimulus with a negative experience).

The Diagnostic and Statistical Manual of Mental Disorders (DSM) is a key resource for classifying mental health disorders; in its various editions, specific phobias have been included and refined. The DSM-III (1980) marked a significant step in systematically classifying phobias. Advances in neuroscience and research have contributed to a better understanding of the neural mechanisms underlying specific phobias, including insights into the role of the amygdala, a brain region involved in processing fear. (Chandan et al.,2024)

3 Common signs and symptoms of phobias

Phobic patients experience intense feelings of anxiety, but only in certain circumstances that frighten them. People with phobias often avoid situations that make them anxious, but this avoidance tends to make the problem worse over time. Clinical features vary be-

tween types of phobias, but the most common signs and symptoms presented in phobic disorders include:

- Feelings of panic, dread, horror, or terror
- Recognition that the fears go beyond the actual threat of danger
- Reactions that are automatic and uncontrollable, practically taking over the person's thoughts
- Rapid heartbeat, shortness of breath, trembling, and an overwhelming desire to flee the situation
- Extreme measures taken to avoid the feared object or situation.

4 Aetiology

4.1 Neurobiological theory

In simple animal phobias, phobic anxiety was imaged by acquiring blood flow scans during exposures to the feared animal. During the initial fearful scans, flow increased in the lateral orbital-anterior insular cortex, bilaterally, the pregenual ACC, and the anteromedial cerebellum ,areas where CBF also increases in other anxiety states . During the development of habituation to phobic stimuli, the magnitude of the hemodynamic responses to the phobic stimulus diminished in the anterior insula and the medial cerebellum, but it increased in the left posterior orbital cortex in an area where flow had not changed during exposures that preceded habituation . The magnitude of the CBF increase in this latter region was inversely correlated with the corresponding changes in heart rate and anxi-ety ratings. As discussed earlier, the posterior orbital cortex was a site where CBF increased in subjects with OCD during exposure to phobic stimuli, with the increase in flow inversely correlated with obsessional ratings. (Davis et al,.2002)

Early neuroimaging studies of fear conditioning, as well as more recent experiments, have found evidence of an activation of the amygdala, the anterior cingulate cortex, and the insula— when healthy participants are confronted with conditioned fearevoking stimuli independent of the task design . These structures are commonly referred to as the "fear network," which is activated during the acquisition phase of fear-conditioning or corresponding paradigms, and shows stronger activation during extinction learning . The amygdala, an important structure for reward learning, processing of socially and emotionally relevant stimuli, and fear acquisition , shows stronger activation to conditioned vs. unconditioned fear-evoking stimuli in healthy controls. However, a more general approach assumes a state value-determining function of the amygdala. According to this approach, the amygdala calculates and holds a continuously updated representation of value . Additionally, studies suggest that the amygdala is also involved in extinction learning in conjunction with the prefrontal cortex (PFC) . Apart from the amygdala, the anterior cingulate cortex and the insula are activated during fear conditioning. The insula, responsible for sensorimotor processing, socioemotional processing, as well as higher cognitive functions, also holds representations of aversive body states (especially the left insular cortex). The anterior insula receives input from the amygdala and projects to the amygdala in turn. The main function of the anterior insula is thought to be the integration of internal states, whereas the posterior insula is responsible somato-visceral integration. Thus, the insula might integrate the somato-visceral sensations from anxiety inducing stimuli with the aversive stimuli in the environment.(Hinze et al.,2021,p.2)

4.2 Classical conditioning theory

A number of contemporary theories concerning the etiology of specific phobias derive from the classical conditioning paradigm. The original learning conceptualization incorporated Pavlovian conditioning principles and stemmed from an influential study by

Watson and Rayner (1920). It was found that by pairing a neutral stimulus with an aversive noise, a conditioned fear response could be established to the previously neutral stimulus. This conditioning explanation was extended by Mowrer's (1939) two-factor theory of fear and avoidance which posited that once a neutral object or situation acquired fear-evoking properties it subsequently developed motivating capacities. Mowrer argued that fear reduction following avoidance acts as a reinforcer and serves to 'stamp in' new behavior. This theory was used to explain the avoidance behavior typifying phobic individuals. Support for the classical conditioning theory of fear has come from a number of sources. First, the results of a multitude of experiments using laboratory animals have proved consistent with conditioning theory . Also, observations of people involved in military combat have demonstrated that traumatic experiences often lead to the development of fears . Finally, several studies have found that a majority of phobic individuals consider classical conditioning experiences as being central to their fear acquisition . A veritable explosion of research into the neural basis of emotion now underpins the classical conditioning account of fear acquisition. In particular, the role of both the amygdala and the hippocampus have been found to play critical and distinctive roles in fear conditioning processes . However, while both interesting and instructive, the relatively recent confirmation of neurobiological changes resulting from fear conditioning is, in itself, insufficient to explain the various complexities of fears and phobias as experienced by individuals. .(Armfield,2006,p.747)

4.3 The preparedness theory

Organisms are likely to be conservative in their dealing withpotentially fatal situations .Given the lurking deadly consequences of failures to elicit fear responses, the evolutionary perspective makes it likely that organisms quickly (i.e., with minimal training) would learn to fear potentially deadly stimuli. These premises were incorporated intoa theory of fear acquisition by Seligman . This theory combined the insight that

intense fear may result from Pavlovian conditioning (e.g., Watson & Rayner, 1920), the evolutionary requirement of survival contingencies, and the empirical fact that phobias primarily occur to stimuli that are survival relevant in an evolutionary perspective (e.g., Marks, 1969). Seligman assumed that evolutionary pressures have predisposed primates to condition fear more readily to stimuli related to recurrent survival threats (phylogenetically fear-relevant stimuli) than to stimuli that never have threatened survival (fear-irrelevant stimuli) or to fear-relevant stimuli that emerged only recently in our evolutionary history (e.g., ontogenetically fear-relevant stimuli such as guns and electric outlets). Seligman (1970) further proposed that prepared associations not only should be easy to acquire (often in as little as one trial) but also should obey different laws of learning than do nonprepared associations For example, he proposed that prepared associations, relative to nonprepared associations, should be more resistant to extinction—another index of robust conditioning important for associations with survival relevance. Seligman and Hager (1972) added that different cognitive mechanisms and physiological substrates also varied with the preparedness dimension, with prepared associations being less "cognitive" (e.g., less influenced by rational input; p. 5) and being mediated by brain areas of more ancient evolutionary origin.(Ohman and Mineka,2001,p.488)

In sum, primates and humans have a biological preparedness to rapidly associate certain kinds of objects- such as snakes, spiders, water and enclosed spaces with aversive events. It has been suggested that this preparedness may have been a selective advantage (e.g., helped in survival) for our ancestors in the course of evolution . Ohman (1996) has provided two lines of evidence to support the preparedness theory of phobias. First, in case of human participants, fear was conditioned more effectively to fear relevant stimuli such as snakes and spiders than to fear irrelevant stimuli such as flowers and vegetables. In case of primates, lab reared monkeys with no prior experience to fear relevant stimuli also showed conditioning for fearing relevant than irrelevant stimuli.(

Gulgoona Jamal and , Zakhir Hussain,p.53)

4.4 Rachman's reconceptualization of classical conditioning theory

After a thorough examination of the literature, Rachman (1976, 1977, 1991) also proposed a number of arguments against accepting the traditional classical conditioning theory of fear, which he believes, at best, can only provide a partial explanation for the genesis of some fears . With respect to the characteristics of phobias these arguments relate to the inability of classical conditioning theory to account for (1) the failure of some people to acquire fear in fear-evoking situations, (2) the uneven distribution of fears in the phobic population, and (3) the finding that phobias and fears could apparently be acquired vicariously or through the reception of symbolic information.

In response to these apparent inconsistencies, Rachman (1977, 1990, 1998) proposed that there are three pathways to fear and that these can be seen as different ways of acquiring beliefs about the existence of fear-relevant contingencies. The three pathways are believed to be classical conditioning, vicarious acquisition through direct or indirect observations, and informational acquisition. In support of Rachman's proposal, several studies have shown that a high percentage of phobic subjects attribute the origin of their fear to either one of these pathways or to a mixed pathway. The veracity of these self-reports has been given support by primate studies which have demonstrated that witnessing another monkey act fearfully towards a stimulus may lead to fear acquisition.

Despite support for Rachman's theory, research that has also used a non-phobic control group has found either few or no differences between the learning histories of fearful and non-fearful subjects .In some cases the experience of pain or aversive events is related to less rather than to more fear. These results indicate that association-based learning experiences, despite the important status attached to them in the literature, do not effectively differentiate fearful from non-fearful individuals. The mechanisms and

reasons underlying fear acquisition are,therefore, in need of explication for it is these factors, and not the experience of a learning event per se, which seem important in determining a person's fear response. Indeed, it seems fair to conclude that learning experiences along the line of Rachman's three pathways are not causes of fear or anxiety but merely serve as opportunities for the potential development of anxiety.(Armfield,2006,p.749)

4.5 Bandura's self-efficacy theory

One of the major cognitive theories of specific phobias has been put forward by Bandura (1977, 1983) who proposed that a person's self-efficacy or perceived ability to perform specific, effective courses of action, as well as their expectations about the likely outcomes of such actions, are major determinants of action. In relation to phobias it is argued that a person's self-efficacy in performing an action related to the phobic stimulus is an important causal factor in the ability to actually perform that action. Several studies have provided support for the self-efficacy theory of phobic behavior. Despite the support for self-efficacy theory, there are a number of problems with its use in explaning the etiology of specific phobias. First, studies investigating self-efficacy theory have failed to establish the direction of causality between self-efficacy cognitions and behavior. For example, experimental manipulations of self-efficacy have tended to use procedures such as modelling which, according to social-learning theory itself, would be likely to affect phobic behavior. Second, the validity of self-efficacy as a cause of behavior has yet to be established. Third, concentration of self-efficacy theory on phobic behaviors ignores the importance of anxiety and fear which are, by definition, critical features of specific phobias. Finally, self-efficacy theory is incapable of explaining some of the characteristics associated with specific phobias, such as the uneven distribution of feared stimuli. For these reasons self-efficacy theory currently represents an inadequate conceptualization of the genesis of phobic fears. (Armfield,2006,p.752)

4.6 Cognitive theory

Cognitive factors, such as attention, memory, cognitive biases help to maintain the phobias that have been acquired. Generally, people with specific phobias tend to pay more attention to threatening information that relates to their fear . For example, individuals with spider phobias are often the first people to spot a spider if there is one in the room. People with phobias also tend to have distortions in their memories for encounters with the objects and situations they fear. For example, people with an animal phobia may remember the animal that they have encountered as larger, faster, or more frightening than it was. Further, people with specific phobias tend to hold beliefs and to interpret situations in such a way as to maintain or increase their anxiety . For example, people with a fear of height may assume that they are more likely to fall. People who fear enclosed places, such as elevators, may believe that they will run out of air, or that they will be unable to escape. Lastly, avoidance of feared situations prevents people with specific phobias from learning that the situations they fear are not as "dangerous" as they feel. In addition, relying on "safety behaviors" (e.g., driving extra slowly to avoid an accident, always wearing shoes to prevent insects from touching one's feet) can also help to maintain a person's fears. .(Gulgoona Jamal and , Zakhir Hussain,p.53)

Conclusion

Despite being common, anxiety disorders are often underdiagnosed, leading to significant functional impairment and psychological distress for affected individuals. Effective treatment typically involves a combination of antidepressant medication and psychological therapies, particularly Cognitive Behavioral Therapy (CBT). Understanding these therapeutic approaches is crucial for clinical psychology students to ensure comprehensive care, promote early intervention, and improve patient outcomes.

Unit 2: Obsessive-Compulsive & Related Disorders

Obsessive-Compulsive Disorder (OCD)

Objectives

By the end of the lecture, students should:

- Have a comprehensive understanding of OCD , its mechanisms.
- Understood the basic definition and symptoms of OCD, distinguishing between obsessions and compulsions.
- Recognize clinical symptoms as well as different types of OCD.
- Gained knowledge about the etiology of OCD, including genetic predispositions and neurological factors involving specific brain regions and neurotransmitters.

Introduction

Obsessive-Compulsive Disorder (OCD) is a prevalent condition that frequently coexists with other disorders. Initially categorized as a neurosis, then as an anxiety disorder, it is now classified under obsessive-compulsive and related disorders. Psychological theories have offered various explanations for OCD, but recent advancements have integrated neuroanatomical, neurochemical, neuropsychological, genetic, and phenotypic data. This has led to the identification of multiple pathological factors, including dysfunctions in cortical-subcortical pathways.

1 Definition of OCD

According to the American Psychiatric Association(2013) Obsessive-Compulsive Disorder (OCD) is a common psychiatric disorder defined as obsession or compulsion, or

both, which causes marked disturbances or interferes with daily functioning. Obsessions are repetitive thoughts, desires, or ideas that are experienced in a disturbing and unwanted way. Obsessions are repetitive behaviors or mental acts that a person feels perform in response to an obsession in a ritualistic way.

The content of obsessions and compulsions varies from person to person; however, recent research on the multidimensional structure of OCD identified 4 common symptoms: 1. Obsession with contamination /compulsion to wash; 2. Accountability for annoying obsessions/compulsion to check; 3. Unacceptable thoughts (sexual, religious, or aggressive); 4. obsessions of symmetry, completion or order/coercion adjustment. Therefore, OCD is essentially a cognitive and emotional processing disorder, in which individuals experience disturbing thoughts, ideas, mental images, and unwanted impulses causing anxiety, which are difficult to eliminate (Pajouhinia et al.,2020,p.234)

2 Historical overview

Berrios (1989) summarized the different historical stages of obsessive disorder in the following phases

Medieval to 19th Century Evolution:

- During the Medieval period, European medical practitioners used Latin terms like obsessio and compulsio, along with local vernacular terms, to describe OCD-like symptoms.
- In the 19th century, French psychiatrists coined terms like manie sans délire and idées fixes but struggled to classify OCD under folie raisonnante due to its non-delusional nature.

Mid to late 19th century developments:

- Post-1850s, OCD was reclassified as "folie avec conscience" (insanity with insight) by the Société Médico-Psychologique, grouping it with disorders like agoraphobia and panic disorder. This classification eventually collapsed due to Kraepelin's restrictive view of psychosis.

Esquirol and volitional monomania:

- Esquirol (1772-1840) classified OCD as volitional monomania, an "involuntary, irresistible, and instinctive activity" not influenced by reason or emotion. By the 1850s, criticisms led to the decline of this classification, which ended with a debate at the Société Médico-Psychologique de Paris in 1853-1854.

Morel's délire émotif:

- In the latter half of the 19th century, Morel (1809-1873) categorized OCD as "délire émotif," a neurosis characterized by fixed ideas and abnormal acts without cognitive impairment. This definition, which allowed for insight, was successful due to Morel's reputation and its classification of anxiety-related conditions. Janet's psychasthenia concept closely aligned with this.

Reclassification and Modern Views:

- Reclassifying OCD as a neurosis revived the idea of nervous system involvement in cognition, emotions, or volition. By 1866, the term "neurosis" was still evolving. In the 1960s, Beech and Perigault, and later DSM-III-R, revisited Morel's view, classifying OCD as an emotional disorder.

Dagonet and the concept of impulsion:

- Dagonet (1823-1902) introduced "impulsion" to distinguish compulsions from obsessions and involuntary actions. Impulsive insanity, including OCD and phobias, was understood both descriptively and explanatorily, favoring internal origins. After monomania declined, Marcé and Foville reclassified impulsive syndromes as impulsive insanity, with Dagonet noting "violent and irresistible impulses."

Legrand du saulle's consolidation:

- In 1875, Legrand du Saulle reported on 27 OCD cases, noting its fluctuating course and classification as insanity with insight. He identified three OCD stages: involuntary thoughts with doubt and brooding, mental representations causing anxiety, and ritual establishment.

Ball's Criteria:

- Ball (1834-1893) suggested eight criteria for diagnosing OCD: insight, sudden onset, paroxysmal nature, fluctuating course, no cognitive impairment, tension relief after compulsions, high somatic and anxiety symptom frequency, and family history. He categorized OCD into minor, moderate, and major severity levels.

Magnan's classification:

- Magnan (1835-1916) classified mental disorders into organic, psychosis proper, and mental retardation. He placed OCD in the psychosis of degeneration category, along with phobias and sexual perversions, attributing these to cerebrospinal pathology and considering them markers of degeneration psychosis. Ameline suggested cerebral entropy as an explanation.

3 Clinical symptoms

OCD symptoms can be classified into partially distinct but also over-lapping subtypes based on their presentation: (1) contamination fears and compulsive cleaning; (2) obsessive thoughts about causing harm and compulsive checking rituals; (3) obsessions with symmetry and compulsive ordering; (4) obsessions with collecting useless objects and compulsive hoarding. (Jalal et al.,2023,p.2)

Obsessions are unwanted ideas, images, or impulses that repeatedly enter a person's mind. Although recognised as being self generated, they are experienced as "egodystonic" (out of character, unwanted, and distressing). Compulsions are repetitive stereotyped behaviours or mental acts driven by rules that must be applied rigidly. They are often intended to neutralise anxiety provoked by the obsessions (table 1.2). They are not inherently enjoyable and do not result in the completion of any useful task. To qualify for the diagnosis, the symptoms must be disabling. Even among children, in whom diagnostic criteria allow less insight, most patients acknowledge the senselessness of the thoughts and behaviours, as well as the wish to be rid of them. (Heyman et al.,2006,p.p224-225)

Table 1.2. Most commmon symptoms of obsessive-compulsive disorder

Obsessions	**Compulsions**	**Mental acts**
• Fear of causing harm to someone else. • Fear of harm coming to self. • Fear of contaminations. • Need for symmetry or exactness. • Sexual and religious obsessions. • Fear of behaving unacceptably. • Fear of making mistake.	• Cleaning. • Hand washing. • Checking. • Ordering and arranging. • Hoarding. • Asking for assurance.	• Counting. • Repeating words silently. • Ruminations. • Neutralizing thoughts.

(Heyman et al.,2006,pp.224-225)

4 Types of OCD

The DSM-5 categorizes various subtypes of Obsessive-Compulsive Disorder (OCD), each with unique characteristics, including checking, contamination, hoarding, indecisiveness, and a need for things to be "just right." Among these, hoarding is notable for its massive accumulation of objects, regardless of their value, leading to clutter and distress due to a compulsive need to save items and distress at the thought of discarding them. The subtype related to contamination involves obsessions and compulsions about real or perceived contaminants, which can be triggered by immoral thoughts, traumatic memories, or mental images, making it one of the most common OCD presentations.

People affected by the “checking” subtype of OCD are engaged in safety checking compulsions, with the main aim of preventing obsessive thinking related to damage, leaks, or harm to other people or oneself and to reduce uncertainty . Typical examples of compulsive checking are verifying that family members are safe, repeatedly retracing the route one drove, and repeatedly checking that doors and windows are securely closed . Checking is often carried out multiple times and can require hours to be completed,

affecting people's lives consistently . "Indecisiveness" is defined by longer decision times as well as by increased searches for information , and the literature shows that it is associated with OCD tendencies and symptoms . People experiencing obsessions postpone or avoid decisions in order to minimize the risk of making mistakes or not being perfect . For example, indecisiveness may affect the amount of time needed for repetition of the compulsive behavior, such as the number of closings needed to actually close the door or knowing when to stop handwashing to be indeed clean . OCD patients may also avoid situations when decision making is required or tend to plan every aspect of their lives to reduce uncertainty . For many researchers , indecisiveness is only a "trait" of OCD patients, but the most used OCD Inventory includes an indecisiveness dimension (i.e., sub-scale) related to OCD symptoms.

"Just right" is an OCD subtype that is characterized by uncomfortable feelings of things not being right. Patients also report feeling driven to perform an action until this uncomfortable sensation subsides, in order to feel things are "just right" . The main symptoms associated with the not-just-right experiences (NJREs) are perfectionism, ordering, symmetry obsessions, compulsions, indecisiveness, and procrastination. We have already addressed indecisiveness in the previous paragraph, showing that procrastination in OCD patients is due to the feeling of imperfection in their actions . In the ordering and symmetry symptoms, the patient does not tolerate objects placed in a disordered or asymmetrical way, even partially. This gives them an unpleasant feeling of lack of harmony and logic . Finally, NJREs are strongly linked to perfectionism , that is, the occurrence of NJREs increases significantly in people that experience maladaptive domains of perfectionism (e.g., concern over mistakes or doubts about actions).(Guazzini et al.,2022,p1109)

5 Aetiology

Obsessive-compulsive symptoms (OCS) play an essential role in OCD's etiology because genetics that contributes to these symptoms undoubtedly impact the brain structure and function that leads to the development of OCD. The primary pathway responsible for obsessivecompulsive behavior is the cortico-striatal-thalamic circuit (CSTC), which links the following brain regions of the orbital frontal cortex, the caudate nucleus, and the thalamus . This neural feedback loop facilitates repetitive thoughts and behaviors through "a series of dysfunctions within the circuits at both the cortical and subcortical levels" . Additionally, the basal ganglia are also implicated to be responsible for OCS. The basal ganglia are a group of nuclei that connect the cerebral cortex, thalamus, and brainstem. According to Mercadante et al, the basal ganglia of those suffering from OCD do not filter cortical impulses properly; thus, the excitatory impulses prohibit the individual from removing worries.

In terms of environmental factors that contribute to the etiology of OCD, one should consider various risk factors. Although not enough research has been done on environmental triggers for OCD, it is evident that several environmental risk factors interact with genes to cause OCD. The first environmental factor is "streptococcus infection" which is any type of infection caused by the spherical bacteria of streptococcus . This type of infection varies in severity, from mild throat infections to pneumonia. According to Swedo (2002), streptococcal infections led to the onset of OCD symptoms in children because their abnormal response to the infection led to self-antibodies and inflammatory changes in the basal ganglia, an area associated with them with OCS (as mentioned previously). The second environmental factor contributing to OCD is "stressful and traumatic life events".(Yang,2022,p.2)

Concerning the neurobiological basis of (OCD), Sean A. Sassano-Higgins, and Michele T. Pato.(2015) demonstrated that the brain regions most involved in OCD are those that

assist with regulation of emotion and cognitive control, and the alterations in these structures potentially mediate the anxiety and misappraisal of threat exhibited by those with OCD. Meta-analytic research has synthesized the discrepant results, finding a smaller combined (white+gray matter) volume of the anterior cingulate cortex (ACC) and orbitofrontal cortex (OFC) , and an increased combined thalamic volume in patients with OCD relative to control participants. Although data are very limited, increased combined thalamic volume has been found to correlate with an increased severity of obsessions and compulsions. Gray matter density has been found in meta-analyses to be reduced in the dorsolateral prefrontal cortex , OFC , dorsomedial prefrontal cortex (DMPFC) , and ACC in patients with OCD relative to control participants. In contrast, gray matter density has been found to be greater in the putamen , caudate , and anterior prefrontal cortex in patients with OCD relative to control participants. In addition to gray matter reductions, white matter density was found to be reduced in the DMPFC and ACC.

It may be even more crucial to consider the functional connections between brain areas involved in OCD than simply their volumes. These connections, known as the corticobasal ganglia-thalamocortical circuitry and the corticostriatal-thalamocortical circuitry, show significant findings. Functional MRI studies have shown increased coordinated activity, or hyperconnectivity, between the ventral caudate/putamen/nucleus accumbens and the anterolateral and medial orbitofrontal cortices in OCD patients. The degree of this activity has been linked to the severity of OCD symptoms.

6 Theories of OCD

6.1 Behavioral-Cognitive Theory

According to Mowrer's two-stage theory of fear and its maintenance, the behavioral theory of OCD suggests that individuals initially develop anxiety or discomfort through

associations between these feelings and a previously neutral stimulus. Through the process of conditioning, this neutral stimulus transforms into a conditioned anxiety trigger, prompting the person to develop avoidance and escape behaviors. These behaviors are reinforced and sustained over time because they effectively reduce the initial anxiety. In essence, a neutral stimulus becomes a conditioned fear stimulus through classical conditioning, and this fear is maintained through negative reinforcement.

On the other hand the cognitive theory suggests that in obsessive problems, intrusive thoughts are seen as signs of personal responsibility for harm to oneself or others. This perception leads to anxiety, depression, and compulsive behaviors like checking and washing to neutralize the threat. These actions, in turn, increase the likelihood of further intrusions and a heightened sense of responsibility, creating a vicious cycle of negative thoughts and compulsions. Interpretations of responsibility also trigger selective attention, reasoning errors, and the need for reassurance, all of which help maintain the intrusive thoughts and the belief in inflated responsibility.(Doron & Kyrios,2005,p.417).

The cognitive-behavioral theory of the development of OCD is, as its name implies, a combination of the behavioral and cognitive theories of OCD. It springs, like all such theories, from an understanding of the role that cognitions play in our behavior, and the subsequent impact behaviors have on cognitions.The cognitive-behavioral model proposes that obsessions and compulsions arise from dysfunctional beliefs that one holds: the greater the strength of the beliefs, the greater the chance that a person will develop OCD. One of the major research findings to support this idea is that unwanted cognitive intrusions are experienced by most people, with similar contents to clinical obsessions, but are not believed and as such cause little to no distress. Conversely, in people with OCD, these intrusive thoughts can become obsessions if they are appraised as personally important, highly unacceptable or immoral, or posing a threat for which the individual is personally responsible. These types of appraisals will lead to high amounts of distress, which one then attempts to alleviate via compulsions. These compulsions result

in anxiety reduction, but it is only temporary and actually reinforces the maladaptive beliefs that led to the negative appraisal in the first place, thus perpetuating the cycle of obsessions and compulsions.(Lack & Huskey,2015,p.28)

6.2 Bio-Psychosocial Models

Dinn et al. (1999) presented a three-factor causal model of OCD, which posited that exposure to long-term, non-specific traumatic stress generates an excessive amount of anxiety during the psychological development of the premorbid OCD child. These individuals with OCD experience alterations in brain metabolism, as a result of the exposure to protracted threat. These alterations affect the basal ganglia-orbitofrontal circuit of the brain, which enters into a state of enhanced responsiveness over time, drastically reducing the threshold for stimulation. In this way, the child becomes hypersensitive to cues that signify potential harm or danger, both external and internal, referred to as 'exaggerated threat appraisal'.

Further to the theory that childhood exposure to traumatic events leads to the development of the magical thinking, superstition and paranormal beliefs of OCD, the three-factor causal model postulated that the child evolves a distinct cognitive style, characterised by exaggerated threat appraisal and thought suppression . Thought suppression refers to efforts to block out obsessions, leading to a paradoxical increase in their intensity and frequency . Because these negative, intrusive thoughts and obsessions arouse extremely high levels of anxiety or disgust, this serves to further intensify their frequency and severity, resulting in a feedback loop. The individual adapts to this hypersensitivity and anxiety by using a variety of strategies constituting the symptoms of OCD.

Conclusion

Obsessive-Compulsive Disorder (OCD) is defined by persistent obsessions and compulsions that interfere with daily functioning. Obsessions are intrusive thoughts that increase anxiety, while compulsions, or rituals, are repetitive behaviors aimed at reducing this anxiety and eliminating the obsessive thoughts. These rituals can be mental or physical, such as repeated hand washing or checking. OCD significantly impairs a person's quality of life, affecting both personal and professional domains, and it is often accompanied by other mental health disorders.

Unit 3: Somatic Symptom & Related Disorders

Hysteria/Conversion Disorder

Objectives

By the end of this lecture, students will:

- Gain a comprehensive understanding of the historical background of hysteria.
- Attain an in-depth knowledge of the clinical aspects of Conversion Disorder as recognized in the DSM-5.
- Understand and explain the causal factors of Conversion Disorder.
- Analyze the causal factors from a multidisciplinary perspective, integrating insights from psychology, neurology, and other relevant fields.

Introduction

Hysteria has been one of the oldest and most enigmatic concepts in medicine, intriguing psychiatrists and neurologists throughout history due to its diverse physical symptoms and fluctuating mental states. At its most extreme, hysteria could manifest as psychosis. Historically, the term "hysteria" encompassed a wide range of loosely related disorders, such as neurological conversion symptoms, dissociative fugue, amnesia, and anxiety hysteria. Recently, the term “functional neurological symptom disorder” has emerged as the preferred diagnostic label. This name is meant to capture the idea that the relevant pathways are structurally intact but functioning abnormally—which is to say, there is a clear difference in brain function in these patients. Of note, a psychological cause may or may not exist and is not required for DSM-5 diagnosis.(Madva et al.,2019,p.3)
The DSM-5 (2013) refers to what was historically known as ’hysteria’ as ’functional neurological symptom disorder, and the revised vertion ’ DSM-5-TR (Text Revision)

categorized functional neurological disorder under **'Somatic Symptom and Related Disorders'**.

1 Definition

Sigmund Freud, a renowned psychologist, first used the term "conversion disorder" and proposed that its symptoms are a reflection of unconscious conflict. The term "conversion" describes the replacement of a suppressed idea with a somatic symptom.Conversion disorder, now known as functional neurological symptom disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-V, is characterised by a sensory or motor function deficit that cannot be attributed to a physical condition, with psychological factors thought to be related to the deficit because symptoms are preceded by conflicts or other stressors. (Bhushan et al, 2023,p.313)

2 Historical Aspects

The first description of conversion disorders is found in ancient times of Hippocrates and Galen. Greek physicians, who considered the symptoms to be specific to women, called it hysteria, which meant “a wandering uterus, hustera.” The term conversion was first used by Freud and Breuer to refer to the substitution of a somatic symptom for a repressed idea. This introduced the psychological concept of primary gain, (i.e., psychological anxiety is converted into a somatic symptom), and secondary gain of such a reaction is the subsequent benefit that a patient may derive from being in the “sick role“. Conversion disorder has always remained at the interface between neurology and psychiatry since the days of Charcot, Breuer, and Freud.

Like any poorly understood phenomenon or disorder, there are many theories explaining the development of conversion disorders, namely, psychodynamic, behavioural,

learning, sociocultural, philosophical, and neurobiological. Conversion disorder is conceptualised as a disorder of the brain associated with disordered emotions, in those with certain personality traits and inappropriate coping to stress, which helps the person avoid the stress rather than face (Chaturvedi & Parameswaran, 2015, p. 114)

3 Clinical Symptoms

According to Janet, the major symptoms of hysteria were somnambulism, double personalities,convulsive attacks, contractures, paralyses, anesthesia, and hysterical stigmata, as well asdisturbances of speech, vision, alimentation, and respiration. Janet (1920, 1925) promoted the concept that ideas and affects may be lost to consciousness, but somehow continues to exertsensory and motor effects via unconscious mechanisms. Janet held Charcot's views on the degenerative neural basis for hysteria.(Maldonado & Spiegel, 2001)

Nowadays, symptomatic neurological functional disorder (conversion disorder) can present with:

- Nonepileptic seizures
- Weakness and paralysis
- Movement disorders
- Speech disturbances
- Globus sensation
- Sensory complaints
- Visual symptoms
- Cognitive symptoms. (Jon Stone Michael Sharpe,2024).(would be explained later)

4 Nosological Classification

FND is classified as “conversion disorder/functional neurological symptom disorder” in the chapter “Somatic Symptom and Related disorders, codeF44.X” in the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5). In the ICD11 (International Classification of Diseases), FND is classified as “dissociative neurological symptom disorder” in the chapter “Mental, Behavioural or Neurodevelopmental Disorders, code 6B60.X,” as well as in the chapter “Diseases of the Nervous System, code 8A0X” under the term “movement disorder for parkinsonism, dystonia, and tremor”.This variability within and across classification systems is problematic, as it perpetuates a cartesian dualism and creates coding problems between mental health and neurological disorders that affect which clinical services will be reimbursed, or by which expert patients should be evaluated in medico-legal cases.(Aybek & Perez, 2022, p.1)

5 Clinical Subtypes Of Conversion Disorder/ Functional Neurological Symptom Disorder « FND »

Historically, the most common conversion symptoms were paralysis, somnambulism, convulsive attacks, and afflictions of the senses, as in blindness and mutism. Nevertheless, conversion disorder may mimic many neurological, medical, and psychiatric disorders. DSM-IV-TR recognizes four conversion disorder subtypes based on the nature of the presenting symptom, These include conversion presenting with primarily motor symptoms or deficits, sensory symptoms or deficits, seizures (e.g., pseudoseizures), and mixed presentations of these symptom.(Maldonado & Spiegel, 2001). According to Varley et al. (2023) FND encompasses functional movement disorder (FMD) ,paralysis, blindness,and non-epileptic seizures(PNES).

Here we summarize the most important subtypes according to the state of the art .

5.1 Functional Movement Disorder(FMD)

(FMD) are frequent and disabling. They include mainly tremor, dystonia, myoclonus and parkinsonism and belong to a larger entity called functional neurological disorders (FND).FND comprise neurological symptoms that cannot be explained by a classical neurological disease. Consequently, FND are embodied by a broad phenomenological spectrum that encompasses non-epileptic seizures, sensorimotor deficits, gait abnormalities as well asabnormal movements.

Classically, onset of FMD is sudden and often with a precipitating trigger . The course of the disorder includes periods of remission (which may be complete) and is variable over time,with worsening and sometimes even a change in the nature of the disorder . A “selective”handicap for a certain type of activity is often present, reflecting discordance with the physical examination of the patient and the socio-professional impact of the disorder. In general, FMD are inconsistent, with variability, distractibility and the possible presence of entrainment.

Recently, the “whack-a-mole” sign has been described, whereby, if the involuntary movements of one body part are suppressed by holding it, then the involuntary movements will migrate to other limbs, and possibly even occur with greater magnitude. (Galli et al, 2019, p.p1-3).Among the different types of functional movement disorder we mention :

- **Functional Tremor:** Tremor is the most frequent FMD presentation, occurring in40% to 50% of persons diagnosed with FMD.Functional tremor can occur in any body part, often with hands and arms most affected. Several clinical examination maneuvers are helpful for diagnosing functional tremor, particularly when assessed in combination.Unlike in other causes of tremor, distraction maneuvers including contralateral limb ballistic movements, mental tasks, patterned contralateral finger tapping and the cranial nerve examination, result in temporary

improvement or abatement of functional tremor.

- **Functional Dystonia :** Functional dystonia is the second most common presentation of FMD.There are 3 distinct presentations that have been described: functional cranial dystonia, functional fixed dystonia, and functional paroxysmal dystonia.

- **Functional Jerks and Myoclonus :** Functional jerks and myoclonus account for 13% to 20% of FMD.Propriospinal myoclonus is a well-defined presentation of functional myoclonus characterized by flexor arrhythmic jerks involving the trunk, hips, and knees, occasionally with associated vocalization. These jerks are often stimulus sensitive and worsen in a supine position.(Gilmour et al,2022,p.p50-51).

5.2 Psychogenic Nonepileptic Seizures (PNES)

Psychogenic nonepileptic seizures (PNES) are periods of abnormal behaviour and experience typically involving impairment of consciousness, flaccid or rigid collapse and/or tremulous limb movements . Their subjective and objective manifestations superficially resemble epileptic seizures, but PNES are not associated with the abnormal electrical activity in the brain which characterises all forms of epilepsy. In view of the paroxysmal nature of both epilepsy and PNES, tests carried out between seizures (such as structural brain scanning or electroencephalography, EEG) usually fail to provide clear diagnostic pointers, and most patients with PNES are initially misdiagnosed as having epilepsy. In those with sufficiently persistent and frequent seizures a definite distinction from epilepsy is ultimately possible by the simultaneous recording of seizure manifestations using video and electrocardiography and EEG demonstrating the absence of ictal electrical changes during PNES.

The overwhelming majority of PNES are reported by patients as being beyond their

voluntary control, and most fulfil the diagnostic criteria of dissociative (conversion) disorder (ICD-10) or conversion (functional neurological symptom) disorder (DSM-5). Controversy exists over the most appropriate name for these events and the disorders they characterise.

The term PNES is most commonly used in the recent scientific literature, as it is more specific than other terms that also encompass non-epileptic episodes with recognised physiological causes. The term is potentially problematic, however, as it makes (arguably unsubstantiated) presumptions about the etiology of these events, whilst maintaining an unhelpful narrative about the distinction between mental and physiological processes. The term "functional seizures" has been suggested as an alternative, but has not entered popular usage amongst epileptologists for whom "functional" has quite different implications to those intended within psychiatry. For that reason, we have elected to follow common practice in the field by adopting the term PNES here. We regard the term as synonymous with "dissociative seizures", "conversion seizures", "nonepileptic attack disorder" and (historically) "pseudoseizures" and "hysterical seizures.(Brown & Reuber ,2016,p.3)

According to Reuber & Brown(2017),PNES are not a nosological entity in their own right. Rather, the diagnostic label "PNES" is applied in a range of clinical scenarios in which seizures are thought to have "psychological" causes. Most, but not all presentations, fulfil the diagnostic criteria of Functional Neurological Symptom (Conversion) Disorder in DSM-5 (American Psychiatric Association, 2013), although some may be a feature of another disorder (e.g., Somatic Symptom, Dissociative, Panic, PostTraumatic Stress) or even be deliberately feigned (as in Factitious Disorder).

6 Etiology Of Functional Neurological Symptom Disorder/ Conversion Disorder

The etiology of Functional Neurological Symptom Disorder, formerly known as conversion disorder, is multifaceted, involving various biological, psychological, and social factors. These factors are more prevalent in patients with FND than in those with comparable symptoms due to recognized diseases . However, it is important to note that while these factors may contribute to the disorder, they are not individually causal.(Mavroudis et al,2024,p.3)

6.1 Central Inhibition Theory & Related Brain Regions

Early neurobiological research on conversion hysteria in the 1960s and 1970s found decreased somatosensory evoked potentials (SEP) in affected limbs of patients with sensory loss, which normalized after symptom resolution. Similar findings were observed in visual evoked potentials (VEP) in patients with vision loss, showing improvement after psychotherapy. However, some case reports indicated normal evoked potentials. Ludwig (1972) suggested that conversion symptoms result from corticofugal inhibition of afferent stimulation, a theory that remains a common initial perspective for understanding motor and sensory complaints in these patients.

Over the past three decades, imaging studies have significantly contributed to understanding conversion symptoms. In the 1990s, structural imaging with small sample sizes and case reports aimed to identify potential brain lesions causing these symptoms. As imaging technology advanced, functional imaging gained prominence. Single Photon Emission Computerized Tomography (SPECT) showed hypoperfusion in the contralateral parietal region and hyperperfusion in the contralateral frontal region in a patient with left-sided sensory loss. Positron Emission Tomography (PET) revealed increased

activity in the right anterior cingulate and orbitofrontal cortex (OFC) during movement effort, but no activation in the primary motor cortex in a patient with left hemiparesis. These findings suggest that motor and premotor areas are suppressed during attempted movement. The central inhibition theory evolved with these discoveries, hypothesizing in the 1990s that the anterior cingulate and OFC block the connection between the premotor/prefrontal area and the primary motor cortex, causing motor symptoms by interfering with motor command delivery.

Over the following years, the number of functional imaging studies gradually increased; it has been suggested that subcortical structures may play a crucial role in central inhibition, previously thought to be mediated only by cortical structures. For instance, SPECT studies showed reduced blood flow in the contralateral thalamus, putamen, and caudate when vibration was applied to the affected limbs of seven individuals with unilateral sensory or motor conversion disorders during symptoms. This reduced blood flow returned to normal after recovery (Vuilleumier et al., 2001). Another study found consistent results, showing decreased activity in primary sensory areas and increased activity in other brain regions, emphasizing the involvement of subcortical structures.

In a series of ten cases, increased activity during vibrotactile stimulation was observed in the right paralimbic areas (insula and anterior cingulate), right temporoparietal junction (TPJ), bilateral dorsolateral prefrontal cortex (dlPFC), right orbitofrontal cortex (OFC), right caudate, right ventral anterior thalamus, and left angular gyrus. Additionally, a study on five individuals with vision loss reported suppression in the visual cortex and increased activity in the left inferior frontal cortex, insula, limbic regions, and bilateral striatum during visual stimulation.(Bağcaz et al,2024,p.p282-283)

From another point of view Nusair et al(2017) mentioned that during conversion reactions, primary perception remains intact, with modulation of sensory and motor planning becoming impaired through disruption of the anterior cingulate cortex, or-

bitofrontal cortex, and limbic brain regions. Furthermore, limited functional imagining findings suggest that frontal, cortical, and limbic activation associated with emotional stress may act via inhibitory basal ganglia-thalamocortical circuits to produce a deficit of conscious sensory or motor processing.

Regarding the neurochemical factors involved in functional neurological disorders, Mavroudis et al (2024), and based on several studies, elucidated that In patients with FND, abnormalities have been reported in neurotransmitters such as dopamine, serotonin, and gamma-aminobutyric acid (GABA) . Moreover, the presence of inflammatory markers and microglial activation in FND patients suggests a possible immune-mediated mechanism of symptom generation . FND may also be caused by abnormalities in neuroplasticity, including synaptic plasticity and cortical reorganization, which affect the brain's ability to adapt to environmental stressors and maintain normal neuronal function.

6.2 HPA & Immunological Changes In Conversion Disorder/Functional Neurological Disorder CD/FND

Recent research has explored various mechanisms that could underlie the pathophysiology of Conversion Disorder/Functional Neurological Disorder . J. Ratcliff, C. van der Feltz-Cornelis(2020) mentioned the activity of glucocorticoids on brain glial cells as one proposed theory for the pathophysiology of Conversion Disorder/Functional Neurological Disorder . Glial and microglial cells, key regulators of the central nervous system (CNS), are sensitive to changes in their environment, including fluctuations in glucocorticoid levels. Glucocorticoids, crucial for homeostasis and bodily regulation, can cause significant health issues, such as multiple sclerosis and dementia, if their concentrations change, either increasing or decreasing. Glial cells have a high number of glucocorticoid receptors, making them susceptible to these changes, which might explain the link between inflammation and CD/FND. Although a direct connection be-

tween glucocorticoids, glial cells, the hypothalamic-pituitary-adrenal (HPA) axis, and FND has not been researched, this theory suggests a potential role of these elements in CD/FND. Additionally, studies indicate that stress, which affects the autonomic nervous system and immune response, might contribute to the development of CD/FND, with evidence pointing to a hyperarousal stress state and the impact of adverse life events on the disorder.

6.3 Psychoanalytic Theories

Psychoanalytic explanations of conversion disorder emphasise unconscious drives, including sexuality, aggression or dependency, and the internalised prohibition against their expression. A classic paradigm of this theory is the case of Anna O., who was treated by Freud. Physical symptoms allow for the expression of the forbidden wish or urge but also disguise it. Other psycho¬analytic explanations focus on the need to suffer or identification with a lost object .(Owens & Dein, 2006, p. 154)

Freud and Breuer believe there is a quantity of something, which they sometimes call "quota of affect," sometimes "sum of excitations," and sometimes "psychical energy," that is subject to a particular general principle. This general principle is the "principle of constancy:" the mind endeavors to keep the quantity low and constant by "disposing associatively of every sensible accretion of excitation or by discharging it by an appropriate motor reaction" . Thus, excitation can pass from idea to idea, until it facilitates some form of action, whereby it diminishes. These "metapsychological" ideas are fundamental to all of Freud's psychoanalytic theorizing.

The revised theory of hysteria proposed that what lay behind symptoms was the intensification of a prevalent kind of intrapsychic conflict. In the hysteric, strong infantile sexual impulses run up against a powerful aversion-based need to repress such impulses. It is these repressed libidinal impulses that are the driving force behind hysterical symptoms . External events like childhood sexual abuse would vastly increase

the strength of both the libidinal impulses and the repressive force against them, hence making hysterical illness significantly more likely, but they are no longer, for Freud, necessary precursors.

Freud's second innovation was less radical, but nevertheless of theoretical and clinical importance. This was the idea that hysterical symptoms may have both primary and secondary gain. Primary gain has to do with finding an outlet for the libidinal energy released by the trauma. Secondary gain has to do with some further practical benefit to the patient from the ensuing symptom. For example, being by the symptom may have the benefit of freeing the patient from the obligation of work. Such secondary gain reinforces the symptom, making it harder to remove.(Michael,2018,p.p3-4)

6.4 Cognitive-Behavioral Theories

Cognitive-behavioral models suggest that its functional neurologic symptoms may result from cognitive, emotional, and behavioral influences at the subconscious levels of processing. A cognitive-behavioral perspective posits that the genesis of functional neurologic symptoms is often rooted in the subconscious processing of perception and behavior. One model within this framework suggests that these symptoms can emerge from cognitive, emotional, and behavioral factors operating at subconscious levels . Heightened anxiety and vigilance might activate this mental representation to a degree where it supersedes actual sensory input, consequently distorting perception and behavior . Another cognitive behavioral theory revolves around dissociation in functional neurological symptom disorder. Dissociation is experienced subjectively as a detachment from oneself (depersonalization) or the environment (derealization). This state involves altered awareness and integration of thoughts, feelings, memories, and identity, as well as a disruption in the integration of bodily experiences and functions. During dissociation, patients might experience a loss of motor control or sensory awareness . This dissociative state can be triggered by various factors, such as fatigue, panic attacks,

physical injuries , recognized diseases or pain, general anesthesia, or drug side effects. Within this model, symptoms like paralysis or abnormal movement emerge during dissociation, accompanied by a loss of personal connection to bodily movements. The focus on these symptoms, coupled with the fear of their potential implications, might lead to more localized depersonalization, thereby extending the duration of the symptoms. In the case of functional seizures, the initial symptoms of autonomic arousal may escalate to the point where the patient's response is a loss of awareness, appearing as a blackout. Research on patients with functional neurological symptom disorder indicates they might have a reduced conscious awareness of their emotional symptoms, like anxiety, which may explain their tendency to report the physical rather than emotional aspects of these events(Mavroudis et al,2024,p.7)

6.5 The Bayesian Model

The Bayesian model offers a theoretical framework that is increasingly used to conceptualize the pathophysiology of functional neurological disorder (FND) . This model is grounded in the principles of predictive coding and active inference, providing insights into how the brain processes information and how this might go awry in FND. According to the Bayesian model, the brain constantly generates predictions about sensory inputs based on prior experiences. These predictions are then updated by incoming sensory information according to a process known as predictive coding. Active inference refers to the brain's mechanism of minimizing prediction errors by either adjusting its predictions (perceptual inference) or by acting on the environment (active inference).

In FND, there appears to be a disruption in this predictive processing . The model suggests that symptoms arise due to an imbalance in the integration of sensory data and top-down predictions. This disruption can manifest as alterations in perception, sense of agency, and motor control, which are characteristic of FND. The symptoms of FND therefore can be viewed as a result of the brain's inaccurate predictions about bodily

states and motor actions.

The Bayesian model also implicates the processing of emotional and sensory signals in FND. In cases where there is a heightened sensitivity to emotional or interoceptive signals, the brain might generate predictions that are overly influenced by these signals, leading to the characteristic symptoms of FND. This aligns with neuroimaging findings that show altered activity in the limbic and salience networks in FND patients . The Bayesian model is supported by neuroimaging studies that show altered brain activations in areas involved in predictive processing and emotional regulation . This integration of theoretical models with empirical neuroimaging data offers a comprehensive approach to understanding and treating FND.

Understanding FND through the lens of the Bayesian model has significant implications for treatment. It suggests that therapeutic interventions might be aimed at recalibrating the brain's predictive models. For instance, therapies like cognitive behavioral therapy (CBT) may help in modifying maladaptive beliefs and expectations, thereby adjusting the brain's predictions and reducing symptom severity.(Mavroudis et al,2024,p.p8-9)

7 Differential Diagnosis

The diagnostic criteria used by DSM-V and ICD-10 in classifying conversion disorder takes a psycho-social perspective. Both diagnostic systems define the following four features to qualify for conversion disorder:

- Neurological symptoms (motor and sensory) and loss of consciousness.
- No substantial evidence of organic causes that can explain the disease.
- Psychological stressors at the onset of the disease.
- Exclusion of faking symptoms.(Dhruv Beri and K Jayasankara Reddy,2020,p.3)

According to Shahid et al.(2015),Patients with conversion disorder may present with blindness, deafness, pseudo seizures, dystonia, paralysis, syncope, or other neurological symptoms. The presenting symptoms depend on the cultural milieu, the patient's degree of medical knowledge (i.e., individuals with a high degree of medical knowledge tend to have more subtle symptoms and deficits that may closely simulate neurological or other general medical conditions, whereas those with less medical knowledge may have more implausible symptoms), and the underlying psychiatric issue(s).The following paragraphs review several examples of psychiatric disorders that should be ruled out before a diagnosis of conversion disorder is made.

Hypochondriasis: Hypochondriasis is the excessive preoccupancy or worry about having one (or more) serious physical illnesses. This debilitating condition is the result of an inaccurate perception of the condition of body or mind despite the absence of an actual medical condition (e.g., "I know I've got cancer; they just haven't done the right test yet").

Factitious disorder: Factitious disorder is a condition in which a person acts as if he or she has a physical or mental illness when he or she is not really sick. Factitious disorder by proxy is when a person acts as if a person in his or her care has an illness when the person does not. Factitious disorder is considered a mental illness because it is associated with severe emotional difficulties. People with factitious disorder deliberately create or exaggerate symptoms of an illness in several ways. They may lie about or fake symptoms, hurt themselves to bring on symptoms, or alter tests (such as contaminating a urine sample) to make it look like they or the person in their care is sick. Those with factitious disorder have an inner need to be seen as ill or injured without the need to achieve personal or financial gain.

Somatisation: Somatisation is a condition in which a person experiences physical symptoms that are inconsistent with or cannot be fully explained by any underlying general medical or neurological condition. Preoccupation with these symptoms leads to

excessive distress in the patient.

Malingering: Malingering is not a mental disorder; however, psychiatrists and neurologists will likely encounter an individual malingering a psychiatric or neurological illness at some point in their careers. Malingering is defined as intentionally feigning the symptoms of a physical, psychiatric, or neurological disorder in order to achieve personal or financial gain. The individual is fully aware that he or she is feigning the symptoms and has clear knowledge of why he or she is doing it (e.g., for financial gain, recognition, or revenge).(Shahid et al.,2015,p.p30-31)

Conclusion

Conversion disorder is a neurological condition characterized by symptoms that cannot be explained by a known neurological disease. These symptoms can affect motor skills, sensitivity, and can manifest as seizures resembling convulsions. Although no neurological disease can explain these symptoms, they are real and not imagined. They cause significant distress and can hinder normal functioning. It is crucial to recognize that these symptoms are not simulated and are not imaginary.

Unit 4: Schizophrenia Spectrum & Other Psychotic Disorders

Schizophrenia

Objectives

- To have the base knowledge about Schizophrenia.
- Establish the positive diagnosis of schizophrenia based on anamnestic and clinical data.
- Identify the differential diagnoses of schizophrenia based on anamnestic and clinical data.

Introduction

Schizophrenia and other psychotic disorders have a profound effect on a person's educational, occupational, and social functioning, often emerging during the transition from adolescence to adulthood. Upcoming lectures will clarify the clinical features of these disorders, particularly schizophrenia and delusional disorders, identify their underlying pathophysiology, and explore differential diagnoses for the two conditions.

1 Definition

Schizophrenia is a chronic psychiatric disorder with a heterogeneous genetic and neurobiological background that influences early brain development, and is expressed as a combination of psychotic symptoms (such as hallucinations, delusions and disorganization) and motivational and cognitive dysfunctions.(Kahn et al.,2015,p.1)

Schizophrenia represents a chronic disorder whose course generally includes a prodromal phase, an active phase with delusions, hallucinations or both, and a residual phase during which the disorder may be in remission.

2 History Of Schizofrenia

The earliest medical description of schizophrenia symptoms belongs to Haslam and Pinel published in 1809. However, schizophrenia-like syndrome is considered to be rare prior 1800 though the description of uncontrolled behavior and psychosis was common in ancient Greek and Roman. Avicenna described some symptoms of schizophrenia. This condition was called "Junun Mufrit," or severe madness. However, other similar cases of this state are not described during the medieval ages. One of the first historical cases of schizophrenia-like syndrome belongs to Italian priest, writer and cartographer Opicinus de Canistris in the 14th century. His autobiographical work describes his mental disease characterized by mania, self-deprecation and depression. More recent case of schizophrenia-like disorder was described by German sculptor Franz Xaver Messerschmitt in the 18th century. During the Messerschmitt life, his thinking was considered as bizarre and implausible, his behavior included social isolation, loss of employment, mania, and depression. He is famous for the collection of busts called "character heads" with extreme facial expressions that may confirm mental disorder.Rare cases of schizophrenia-related symptoms before 1800 confirm that this mental disease became widespread only beginning from the 19th century.(Hamad,2018)

During the 19th century, psychiatrists described more cases with the same symptoms though the definitions were different. In 1899, Emil Kraepelin improved the classification of mental disorders separating mood disorder and dementia praecox that was characterized by schizophrenia-like symptoms. In 1908, psychiatrist Eugen Bleuler introduced the definition "schizophrenia" which is translated from Greek as "splitting of the mind." He described four main symptoms related to the disease: Flattened affect, autism, impaired association of ideas, and ambivalence. Later, the psychiatrist Kurt Schneider described more detailed symptoms that distinguished schizophrenia from other disorders. They are called first-rank or Schneider's first rank symptoms including,

for example, delusions, voice auditory hallucinations commenting actions or conversations, and inserted thoughts.

During early century, schizophrenia was considered as highly hereditary disorder. Therefore, eugenic psychiatrists including Bleuler tried to control the incidence of the disorder sterilizing or murdering the patients with schizophrenia. In 1970, the schizophrenia concept was estimated once more. New criteria were introduced by psychiatrists Robins and Guze while Schneider's first-rank symptoms became less important. During this period, large amounts of discrepant studies from Europe and the USA were compared to unify the symptoms that helped to develop reliable diagnosis of schizophrenia.

The controversies took place due to different descriptions of symptoms in the DSM-II manual in the USA and ICD-9 in Europe. It was investigated that symptoms of schizophrenia can be found in different countries and cultures suggesting great biological impact to the development of the disease. The WHO data indicated stable similar incidence rate all over the world. In 1970, more than 40 criteria of schizophrenia diagnosis were suggested that are used now.(Hamad,2018)

3 Clinical features

Schizophrenia has varied symptoms that generally begin in early adulthood and usually continue throughout life. Most patients have a history of behavioural dysfunction primarily social and learning difficulties. Diagnostic features of schizophrenia include auditory hallucinations (an experience involving the apparent perception of something not present) and delusions (the action of deluding or the state of being deluded). Patients may have experienced these symptoms but this phenomenon may or may not true and now in its troubling condition. Schizophrenia has different main symptoms which can be divided into different phases which are; Positive, Negative and Cognitive symptoms.

- Positive symptoms are those which can be easily identified and not seen in healthy

people. Such symptoms include Hallucination, delusion and abnormal motor behaviour having fluctuating degree of severities.

- Negative symptoms are can't easily identify and associated with high morbidity rate. The most common Negative symptoms included Avoilition, Alogia, Anhedonia and diminished emotional expression.

- Cognitive Symptoms, being the newest classification. These ultimately impairing the individual's communicating skills by disturbing his speech and attention.(Zafa et al.,2018, p.847)

4 Aetiology Of Schizophrenia

Recent studies on schizophrenia highlight multiple underlying mechanisms, emphasizing the need for a multidisciplinary approach. The section centers on the pathophysiology of this significant psychiatric disorder.

4.1 Pathophysiology Of Schizophrenia

4.1.1 Anatomical Abnormality

Many brain imaging and neuropathological studies have attempted to relate the manifestations of schizophrenia to altered structure or function of particular brain regions and circuits. There has been progress in relating some aspects of the disorder to specific underlying neurobiology and several lines of evidence implicate the involvement of the prefrontal cortex, in particular, in specific cognitive deficits (e.g., working memory and executive control). However, subtle reductions in grey matter and abnormalities of white matter have been found across many brain regions and circuits. The reduction of grey matter progresses with the duration of illness, especially in the temporal lobe, and seems to be associated with antipsychotic treatment. However, even drug-naïve patients

show volume reductions (albeit not as pronounced as treated patients), especially in the caudate nucleus and thalamus. Moreover, despite many hundreds of studies, no circumscribed anatomical or functional abnormalities that are specific to the disorder have been identified. This is likely to reflect the complexity and heterogeneity of the psychopathology and associated cognitive impairments, and the lack of clear boundaries separating schizophrenia from other disorders or wellness. .(Owen et al.,2016,p.7)

4.1.2 Dysfunctional Neurotransmission

There are three main hypotheses regarding the development of schizophrenia. The neurochemical abnormality hypothesis argues that an imbalance of dopamine, serotonin, glutamate, and GABA results in the psychiatric manifestations of the disease. It postulates that four main dopaminergic pathways are involved in the development of schizophrenia. This dopamine hypothesis attributes the positive symptoms of the illness to excessive activation of D2 receptors via the mesolimbic pathway, while low levels of dopamine in the nigrostriatal pathway are theorized to cause motor symptoms through their effect on the extrapyramidal system. Low mesocortical dopamine levels resulting from the mesocortical pathway are thought to elicit the negative symptoms of the disease.

Other symptoms such as amenorrhea and decreased libido may be caused by elevated prolactin levels due to decreased availability of tuberoinfundibular dopamine as a result of blockage of the tuberoinfundibular pathway. Evidence showing exacerbation of positive and negative symptoms in schizophrenia by NMDA receptor antagonists insinuates the potential role of glutaminergic hypo activity while serotonergic hyperactivity has also been shown to play a role in schizophrenia development . There are also arguments that schizophrenia is a neurodevelopmental disorder based on abnormalities present in the cerebral structure, an absence of gliosis suggesting in utero changes, and the observation that motor and cognitive impairments in patients precede

the illness onset. Conversely, the disconnect hypothesis focuses on the neuroanatomical changes seen in PET and fMRI scans There is a reduction in grey matter volume in schizophrenia, present not only in the temporal lobe but in the parietal lobes as well. Differences in the frontal lobes and hippocampus are also seen, potentially contributing to a range of cognitive and memory impairments associated with the disease.(Saparia et al.,2022,pp.66-67))

In sum Dopamine hypothesis proposed that Atypical activity at dopamine receptor sites specifically in D2 is understood to be linked with many of the symptoms of schizophrenia. Four dopaminergic pathways have been involved:

1. The nigrostriatal pathway initiates in the substantia nigra and finishes in the caudate nucleus. Low dopamine levels inside this pathway are understood to affect the extrapyramidal system, causing motor symptoms.

2. The mesolimbic pathway may play a role in the positive symptoms of schizophrenia in the existence of excess dopamine.

3. Negative symptoms and cognitive deficits in schizophrenia are said to be initiated by low mesocortical dopamine levels.

4. A reduction or blockade of tubero-infundibular dopamine outcomes in elevated prolactin levels resulting in galactorrhea, amenorrhea, and decreased libido.

Glutamate hypothesis recommended that disturbed glutamatergic function may add to the biological processes essential some clinical features, in specific cognitive dysfunction.One notion is that glutamatergic dysfunction in schizophrenia is associated to dysfunction of parvalbumin-positive interneurons inside the cerebral cortex and hippocampus, which are subtle to alterations in NMDA-type glutamate receptors. These fast spiking neurons harmonize the firing of pyramidal neurons and cause the production of gamma oscillations, which is vital to proper cognitive function. Subse-

quently, dysfunction of this population of neurons may cause the cognitive deficits seen in schizophrenia.(Fatani et al.,2017,p.2642)

The serotonin hypothesis for the development of schizophrenia emerged as a result of the discovery that lysergic acid diethylamide (LSD) enhanced the effects of serotonin in the brain.Subsequent research led to the development of drug compounds that blocked both dopamine and serotonin receptors, in contrast to older medications, which affected only dopamine receptors. The newer compounds were found to be effective in alleviating both the positive and negative symptoms of schizophrenia.(Patel et al,2014,p.638)

Serotonin (5-hydroxytryptamine;5-HT; C10H12N2O) is a molecule with central and peripherical functions in the human body such as regulating mood and cognitive functions . Imbalances in serotonin concentration have been linked to a range of health conditions such as depression and schizophrenia . The main relationship between serotonin and schizophrenia is that changes in serotonin concentration can contribute to the onset of schizophrenia, and conversely, schizophrenia can gradually affect the serotonergic systems of the brain . Nowadays, there is no consensus on which one comes first. Serotonin is a molecule synthesized predominantly in peripheral tissues by tryptophan hydroxylase-1 (TPH1) and in the central nervous system by tryptophan hydroxylase-2 (TPH2), both from amino acid Ltryptophan (L-Trp). Diverse studies have shown an association between increased concentrations of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) in cerebrospinal fluid (CSF) and family history of schizophrenia . In addition, evidence has demonstrated that the 5- HT1A, 5-HT2A, 5-HT2B, 5-HT6, 5-HT7 serotonin receptors are modified in patients with schizophrenia . Therefore, serotonin is a medical target for many psychiatric and neurological disorders, including antipsychotic treatment (antipsychotic atypical, typical, SSRI, MAOI). Notwithstanding the increasing evidence that dysfunction of serotonin activity in the brain is strongly associated with schizophrenia, other neurotransmitters such as dopamine and glutamate, or other metabolites in the L-Trp metabolism, as well as

kynurenine pathway and its rate-limiting enzymes, might also participate in generating schizophrenia.(Canul-Medina et al,2024,p.p2-3)

4.1.3 Neurodevelopmental Models Of Schizophrenia

The gestational methylazoxymethanol acetate (MAM) model is a developmental disruption model of schizophrenia that involves the administration of MAM to pregnant female rats, on gestational Day 17, which results in neurochemical, behavioral, and anatomical deficits in adult rats that are consistent with those observed in patients with schizophrenia . These include: a reduction in cortical and subcortical volume; increased neuronal cell density in prefrontal/cingulate and insular/perirhinal areas; decreases in the thickness of the PFC, ventral perirhinal cortex, and hippocampus; impairment of pre-pulse inhibition of startle, executive function, and reversal learning; and increased response to amphetamine and PCPincreased locomotion in adult, but not prepubertal rats.

In the MAM model, NMDAR dysfunction appears to arise during the period of heightened epigenetic vulnerability . Epigenetically mediated alterations in NMDAR subunit composition are observed in the prelimbic cortex of juvenile MAMexposed animals . These alterations occur before the emergence of dopaminergic hypersensitivity and cognitive deficits in young adulthood. Thus, developmental animal models, such as the gestational MAM model, can be used to test the extent to which deficits resulting from postnatal glutamatergic manipulations may be rescued by antipsychotic drugs or experimental compounds or environmental interventions at different periods during brain development and in adult animals. Furthermore, it may also be possible to determine from these models whether, theoretically, glutamate activity might be rescued pharmacologically in people showing early signs of psychosis in young adulthood.

In the MAM model, increased excitatory input from the hippocampus to the nucleus accumbens reduces inhibition of the ventral pallidum and leads to increased population activity of dopaminergic neurons projecting to the striatum . In this psychosis model, striatal dopaminergic hyperfunction is driven by the hippocampus and glutamate is critical in this process MAM rats show a reduction in parvalbumin (PV) interneuron density throughout the medial PFC (mPFC) and the ventral hippocampus that impacts gamma oscillations during task performance . In people at clinical high risk (CHR) for psychosis, resting blood flow and activity in the hippocampus are also increased, and may be related to mPFC GABA levels . Schobel et al., observed that hypermetabolism in the CA1 sub region of the hippocampus spread to the subiculum after psychosis onset in patients at CHR and predicted hippocampal atrophy. As acute ketamine produced similar pattern of hypermetabolism in mice, these findings may be linked to NMDAR hypofunction. Postmortem studies in schizophrenia describe a selective loss of GABAergic PV interneurons in the hippocampus and frontal cortex , and a corresponding deficit in GABAergic signaling may also contribute to hyperactivity within the hippocampus.(Egerton et al,2020,p.61)

4.1.4 Neurobiological factors

No single area of the brain is likely to account for all symptoms of schizophrenia, and several imaging modalities, such as MRI, magnetic resonance spectroscopy (MRS), positron emission tomography (PET), functional MRI (fMRI), diffusion tensor imaging (DTI), arterial spin labeling (ASL), and neurite orientation dispersion and density imaging (NODDI), among others, have consistently identified abnormalities in brain structure, function, connectivity, and chemistry. Abnormalities are diffuse but are more pronounced in the cortex and subcortical brain regions. Moreover, the origins of these abnormalities have been suggested to occur during early brain development as well as around the time of psychosis onset. Multiple structural abnormalities in schizophrenia

have been identified, including (1) smaller hippocampal volumes followed by a smaller amygdala, thalamus, nucleus acumbens, and overall intracranial volume, (2) larger pallidum and lateral ventricle volumes, (3) widespread cortical thinning, (4) gray matter alterations in frontal, temporal, and cingulate cortices, and (5) abnormalities in white matter connections leading to inefficient communication between functional brain regions. Additionally, these changes, including decreases in overall brain tissue and gray matter density, may worsen during each psychotic exacerbation.

Differences in brain perfusion and metabolism have also been noted in those with schizophrenia in comparison to controls. Individuals with schizophrenia have decreased cerebral blood flow, along with distinct areas of hypoactivation, hyperactivation, and abnormal resting-state brain activity. Despite the myriad of reproducible findings, after neuroimaging has ruled out an organic etiology for schizophrenia symptoms, there are few clinical implications for neuroimaging findings at this time. However, neuroimaging has been suggested as an objective biomarker that could one day assist with diagnostic uncertainty and treatment decisions. Biomarkers could also help to predict the risk for developing psychosis in someone that is in their prodromal phase or is at a high risk to develop schizophrenia. Biomarker targets include gray matter loss, NMDA receptor dysconnectivity in the excitatory/inhibitory balance resulting in altered functional network architecture, dopamine hyperactivity, NMDA hypofunction, hippocampal hyperactivity, and autoimmune or neuroinflammation dysregulation. (Faden & Citrome,2023)

5 Pluralistic Approach To Schizophrenia

Since the early 1980s, the predominant theoretical model in academic American psychiatry has been Engel's biopsychosocial model, which considers biological, psychological, and social factors in the etiology of mental disorder. This was predated by Adolf Meyer's psychobiology in the early 20th century .Nevertheless, much of the research

and scholarly activity on schizophrenia over the course of the past 40 years has been strictly biological in nature. Modern textbooks on schizophrenia may only include short passages on psychosocial approaches which are usually limited to brief, manualized therapies, and psychosocial rehabilitation. Discussions of the psychological aspects of schizophrenia often consider these problems as consequences rather than as causes of the disease. Thus, much of the modern psychiatric literature on schizophrenia lacks the pluralism that is found in writings from the past century. (Ruffalo (2023, p. 226).

6 Schizophrenia in DSM

The definition of schizophrenia has evolved through the six editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM-I, DSM-II, DSM-III, DSM-III-R, DSM-IV, and DSM-IV-TR. Three major roots are reflected in all definitions:

1. the Kraepelinian emphasis on avolition, chronicity and poor outcome.
2. incorporation of the Bleulerian view that dissociative pathology is primary and fundamental and accent on negative symptoms.
3. the Schneiderian stress on reality distortion or positive symptoms.

The relative emphasis paid to these three perspectives has, however, varied over time, with the Bleulerian accent on negative symptoms and interpersonal pathology leading to a broad definition reflected most strongly in DSM-I and DSM-II. This led to a marked discrepancy between the diagnosis of schizophrenia in the USA versus the UK and perhaps much of Europe. In reaction to these inconsistencies, the operationalized criteria of DSM-III narrowed the definition by requiring chronicity and poor function and highlighting Schneiderian first-rank symptoms in an effort to define a more homogeneous disorder. From DSM-III through DSM-III-R to DSM-IV, there has been a modest

expansion of the criteria of schizophrenia with the elimination of the requirement that onset occur before age 45 and inclusion of negative symptoms.

The DSM-IV construct of schizophrenia has been found to be clinically useful, has high reliability, and fair validity . Its validity is supported by a range of antecedent (familial aggregation, environmental risk factors), and predictive (diagnostic stability, course of illness, treatment response) validators ,although concurrent validation (e.g., biological markers) is less robust. DSM-IV schizophrenia has very high diagnostic stability, with 80–90% of individuals receiving an initial diagnosis of schizophrenia retaining that diagnosis at 1–10 years . Therefore, the core of the DSM-IV diagnostic criteria for schizophrenia will be retained in DSM-5, with modest changes proposed principally for the purpose of simplicity and incorporation of new information about the nature of the disorder accumulated over the past two decades. Most persons who did (or did not) meet the DSM-IV criteria for schizophrenia should continue to meet (or not meet) the DSM-5 criteria. The heterogeneity of schizophrenia is, however, poorly explained by the DSM-IV subtypes, necessitating a change in approach.(Tandon et al.,2013,p.2)

In contrast to DSM-IV, in DSM-5 a patient is always required to have at least 2 characteristic symptoms. Thus, the special position of bizarre delusions or Schneider first-rank auditory hallucinations has been omitted, due to the nonspecificity of the Schneider firstrank symptoms and the unreliability of the distinction between bizarre and nonbizarre delusions. Several trials have also demonstrated that the number of patients diagnosed with schizophrenia based on the presence of only bizarre delusions or first-rank auditory hallucinations is low. In addition, in DSM-5, a patient is required to have at least one of the following positive symptoms: delusions, hallucinations, or disorganized speech.(Mattila et al., 2015,p.637)

7 Diagnosis

The diagnosis of schizophrenia is reached after satisfying the criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR). Individuals must have 2 or more of the following symptoms: delusions, hallucinations, disorganized speech, disorganized behavior, and negative symptoms (eg, avolition, anhedonia). Symptoms should be present for at least 1 month, with continuous signs of disturbance for at least 6 months (or less if successfully treated). Additionally, symptoms must be associated with functional impairment. Although the diagnosis can be made using standardized interviewing or scales, such as the Structured Clinical Interview for DSM-5 (SCID-5), clinicians typically assess for schizophrenia by obtaining a comprehensive history, including family history, speaking with collateral sources of information, and conducting a mental status examination. Although psychotic symptoms typically result in the patient first receiving medical attention and may be the most concerning and obvious, any symptom can predominate.

Another method of conceptualizing schizophrenia is as a constellation of symptoms with 3 primary domains: (1) positive (eg, delusions, hallucinations, disorganized thought process), (2) negative (eg, apathy, affective flattening, social isolation, anhedonia), and (3) cognitive (eg, memory, executive function). Schizophrenia is heterogeneous. There is no pathognomonic presentation and individual symptoms vary. However, despite a myriad of distinct symptom presentations, pharmacologic treatment is fairly uniform consisting of antipsychotic medications.

Although psychotic symptoms may be the most apparent, they are often preceded by negative and cognitive symptoms in a period known as by subtle and gradual changes in behavior, personality, and functioning. However, in other cases, the onset of psychosis can occur abruptly in otherwise highly functioning individuals. Characterizing symptoms are important as positive symptoms are much more amenable to treatment than

negative and cognitive symptoms.

At present, there is no blood test for schizophrenia, and as such, schizophrenia is a diagnosis of exclusion. Not all psychosis is schizophrenia, and alternative organic and psychiatric etiologies must be ruled out before a diagnosis of schizophrenia can be reached . (Faden & Citrome,2023)

An inclusive differential diagnosis of schizophrenia is essential to differentiate the disorder from other mental disorders, for example major depressive disorder with catatonic or psychotic features, or schizoaffective disorder, body dysmorphic disorder, or schizophreniform disorder, and post-traumatic stress disorder, and also obsessive- compulsive disorder. Hence schizophrenia can be distinguished from these comparable conditions with the help of a careful examination of the duration of the illness, the period of delusions or hallucinations, and the intensity of depressive and manic symptoms. For instance, in the DSM-5, a patient may meet diagnostic criteria for schizophrenia, but does not necessarily meet the 6 month duration of symptoms; therefore a diagnosis of schizophreniform disorder is provisionally made. If symptoms persevere for 6 months a judgment of schizophrenia is made.

Additionally, the clinician must approve that the offering symptoms are not due to substance abuse or some other medical condition.(Fatani et al.,2017,p.2643)

8 Differential Diagnosis

Diagnosis is made clinically on the basis of history and by examination of the mental state; there are no diagnostic tests or biomarkers. Schizophrenia usually presents with psychosis and the main differential diagnoses, in DSM5, are affective psychoses (bipolar disorder with psychotic features and major depressive disorder with psychotic features), other, closely related, non-affective psychoses (schizoaffective disorder, schizophreniform disorder, delusional disorder, brief psychotic disorder and psychotic disorder not otherwise specified), substance induced psychotic disorders (alcohol induced, other substance induced) and psychotic disorders due to a general medical condition.

Differential diagnosis takes into account the duration of illness, the nature and pattern of associated substance abuse, the cooccurrence of depression or mania and the presence of somatic illness. Schizophrenia, like the majority of psychiatric diagnoses, remains a syndromic concept. The use of operational criteria, such as those embodied in the Diagnostic or Statistical Manual of the American Psychiatric Association (DSM), or the International Classification of Diseases (ICD) of the World Health Organisation has provided a reliable approach to making psychiatric diagnoses in the clinic. However, the assumption that the clinical syndromes defined in this way represent valid disease entities with distinct underlying aetiology and pathogenesis is increasingly seen as having impeded research.

Indeed psychiatric diagnoses have the unusual property of being simultaneously too broad and too narrow. Individuals with a diagnosis of schizophrenia vary greatly in predominant symptoms, response to treatment, course and outcome. However, attempts to resolve this heterogeneity into valid subtypes has repeatedly failed. On the other hand,

many psychiatric diagnoses have symptoms in common and the boundaries between schizophrenia and other disorders are indistinct as are the boundaries between disorder and wellness. With regard to the latter there is an increasing realization that psychotic symptoms, such as auditory hallucinations and paranoid thinking, occur in attenuated form in 5–8% of the healthy population. This has led to suggestions that dimensional approaches to diagnosis and classification might replace or enhance current categorical approaches.(Owen et al,2016,p-p2-3)

Delusional Disorder

1 Definition

Delusional disorder, the contemporary conceptualization of paranoia, is characterized by the presence of one or more non bizarre delusions and the relative absence of associated psychopathology. Delusions are currently subdivided by content and involve experiences that can conceivably appear in real life, such as being malevolently treated (persecutory type), having a physical disorder (somatic type), being loved at a distance (erotomanic type), having an unfaithful sexual partner (jealous type), and possessing inflated worth, power, identity, or knowledge (grandiose type)(O'Connor et al,2007,p.83)

Delusional Disorder is characterized by false beliefs that are held with firm conviction despite counterevidence and are typically accompanied by strong affect and exaggerated vigilance . These delusional beliefs are usually monothematic and encapsulated and lack the bizarreness of delusions found in schizophrenia. Given that delusions represent the main symptom in DD, defining the term becomes essential. The DSM-IVTR considers a delusion as: A false belief based on incorrect inference about external reality that is firmly sustained despite what almost everybody else believes and despite what constitutes incontrovertible and obvious proof or evidence to the contrary. The belief is not one ordinarily accepted by other members of the person's culture or subculture.(Ibanez-Casas & Cervilla, 2012, p. 86)

Oxford Dictionaries online provide two definitions of paranoia. The first definition states that paranoia is "a mental condition characterized by delusions of persecution, unwarranted jealousy, or exaggerated self-importance, typically worked into an organized system" and the other definition states that paranoia is an "unjustified suspicion and mistrust of other people". Perhaps these two definitions reflect the different ways that the experience is understood, and the many meanings the term encapsulates.

A persecutory belief is considered to be the central defining feature of paranoia and includes two essential elements: i) a belief that harm will occur, and ii) an attribution that others intend this harm. In the general population, such persecutory ideas can be experienced with varying degrees of frequency and entertained to varying degrees of intensity. Paranoia can range from mild concerns about others' intentions to beliefs that are sufficiently unlikely, and inflexible to be classified as a psychiatric symptom, most notably, as a paranoid delusion. One of the implicit assumptions about paranoia is that it represents an exaggerated or false attribution of harmful intent to others. However, given the continuum of paranoia, paranoid explanations can, and occasionally should, be accurate although these are likely to be increasingly inaccurate as paranoia becomes more disabling and a likely focus of clinical concern(Raihani and Bell,2019,p.2).

In the most recent version of the DSM (DSM-V), delusional beliefs are (syndromally) defined as distorted or excessive inferences about reality highly resistant to change despite conflicting evidence (APA, 2013).

2 Brief History

The psychopathology and nosology of paranoia/delusional disorder (DD) have been the objects of discussion since the time of Kraepelin, who defined paranoia as a chronic delusional condition where no deterioration or hallucinations occur, unlike dementia praecox (schizophrenia). By contrast, Bleuler classified paranoia as a rare form of schizophrenia in which hallucinations may sometimes occur.(De Portugal et al.,2013, p.243)

Thus , Kraepelin distinguished between dementia praecox (later renamed schizophrenia) and paranoia (later called delusional disorder) on the basis that the former comprised incoherent delusions in a disintegrating personality, whereas in the latter the personality was intact and the delusions coherent. Jaspers (1923/1946) subsequently

made a distinction between the true delusions of schizophrenia, 'which go back to primary pathological experiences as their source, and which demand for their explanation a change in the personality' , and the term delusion-like experiences which is 'reserved by us for those so-called "delusions" that emerge comprehensibly from other psychic events and can be traced back psychologically to certain affects, drives, desires and fears'. Sérieux and Capgras postulated a hypertrophy of attention in which the individual focuses on particular issues to the exclusion of others, recalling the 19th-century concepts of idées fixes.(Christopher F. Fear,2013,p.213)

In 1918, Kretschmer challenged somatogenic and psychogenic theories by suggesting that delusions were derived from the sensitive constitution of a person, Combining psychological and somatic perspectives. However, German psychiatry has largely followed the Schneider model, which excluded paranoia from psychological developments and classified it in the category of «endogenous psychoses», along with manic-depressive psychosis and schizophrenia. Later, Kolle and Bleuler further integrated paranoia into the spectrum of schizophrenia, leading to technical obsolescence of the term and terminological confusion in diagnosis. In the 1970s and 1980s, renewed interest and empirical criteria led to the recognition that paranoia was more common and easier to diagnose. The DSM-III-R restored paranoia under the heading «delirious disorder (paranoid)» in 1987, a categorization maintained in the DSM-IV and the DSM-IV-TR. For more, see (Fear, C. F., 2013, p. 213)

The Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association, 2013) identifies paranoia as a symptom present in various mental health conditions, including paranoid personality disorder, psychotic disorders, schizophrenia and delusional disorder. Additionally, paranoia can also be a symptom associated with other conditions like post-traumatic stress disorder, depression, and social phobia.

Kenneth S. Kendler. (2017), concluded that the clinical concept of paranoia has

evolved considerably over the 20th century, reflecting changes in psychiatric understanding and diagnostic practices. While there has been general agreement on the nature of paranoia following Kraepelin's description, some authors have expanded or questioned this concept. The diagnostic criteria for paranoia and delusional disorders have shifted significantly from DSM-III to DSM-5, moving away from a narrow definition to include a broader range of delusional themes. Despite this evolution, the concept of paranoia remains valuable for understanding certain psychiatric conditions, even with its overlap with broader categories like paranoid schizophrenia. These findings highlight the challenges and complexities in maintaining consistent diagnostic categories over time and underscore the need for ongoing research and discussion in the field of psychiatry.

3 Delusional Beliefs Criteria

Defining delusions and understanding the different psychiatric and medical conditions in which they occur can be difficult due to the differences in the associated symptoms. Many standards have been proposed in psychological literature. In this regard, Oltmanns (1988) suggested a multi-criteria approach to categorizing beliefs as delusional. These criteria are:

- The balance of evidence for and against the belief is such that other people consider it completely incredible.
- The belief is not shared by others.
- The belief is held with firm conviction. The person's statements or behaviours are unresponsive to the presentation of evidence contrary to the belief.
- The person is preoccupied with (emotionally committed to) the belief and finds it difficult to avoid thinking or talking about it.

- The belief involves personal reference, rather than unconventional religious scientific or political conviction.
- The belief is a source of subjective distress and interferes with the person's occupational and social functioning.
- The person does not report subjective efforts to resist the belief (in contrast to patients with obsessional ideas).

The more a belief fits the above criteria then the more likely it is to be a delusion. However it is important to note that none of the dimensions alone constitutes a sufficient criterion.

4 Types Of Paranoia

The term paranoia basically implies a morbid distortion of beliefs and attitudes concerning relationships between oneself and other people and situations. Paranoia, like many other psychological phenomena, can present in an affected person in a variety of ways.

- **Paranoia as a symptom:** This can be an over-valued idea or a delusion. Persecutory type is the most common. Persecutory ideas are common in normal people as an adaptive psychological process, which helps to detect threats to self. Paranoid thinking becomes clinically significant when they become over generalized. Paranoid ideas can be considered as lying in a continuum, which ranges from day to day suspiciousness to clinically significant delusions (3,4). Paranoid ideas occur in 10-15% of the general population, while emotionally distressing paranoia occurs in 5-6%. Prevalence of delusions amounting to a psychotic disorder occur in 1-3%.
- **Paranoia as a syndrome:** Paranoid symptoms can occur as part of another psychiatric disorder, such as schizophrenia, mood disorder or an organic mental dis-

order. Such symptoms occur in delusional disorders where there is no other psychopathology.

- **Paranoia as a personality type:** Mistrust of other people is a cardinal feature of paranoid personality disorder. They are preoccupied with the idea that others want to harm or deceive them. Hence they are reluctant to confide in others for fear of malicious use of the information given. They perceive innocent incidents as threatening. Such paranoid ideas may range from overvalued ideas to full blown delusions.(Perera et al.,2010, p.42)

In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders, seven subtypes of delusional disorder are listed.

1. **Persecutory type:** A preoccupation with the belief that one is being persecuted or conspired against.
2. **Somatic type:** A conviction that one's body is defective or infested or malformed.
3. **Jealous type:** A conviction that one's lover is unfaithful.
4. **Grandiose type:** A belief that one is somehow superior to others.
5. **Erotomanic type:** A false belief that one has aroused the passionate love of someone important.
6. **Mixed type:** False beliefs that combine the above themes.
7. **Unspecified type:** A vagueness in the expression of one's beliefs that does not permit sub-classification.

5 Theoretical Approach

5.1 Psychoanalytic & Psychodynamic Contributions

Freud first took up the subject of paranoia in Draft H (January, 1895). He stressed that paranoia was a pathological mode of defense, and, after giving a clinical example, stated that the core of the case was that the patient was sparing herself from a self-reproach and that the result of the defense was that the same charges reached her now from the outside, people were saying what she would have otherwise have said about herself, and in this form, the reproaches could be rejected. Freud noted that either paranoia or its contrary, megalomania, would serve the purpose of defense but that "in every case the delusional idea is clung to with the same energy with which some other intolerable, distressing ideas is fended off from the ego. Thus these people love their delusion as they love themselves".

In Draft K (January, 1896) he again proposed that paranoid formations arise in the place of a self-reproach, that is, the paranoid becomes distrustful and over-sensitive to people because he feels they are, in some way, accusing him. He adds to his formulation that, if the ego is overwhelmed, the paranoid process reaches its conclusion either in "melancholia (a sense of the littleness of the ego), which, in a secondary manner, attaches to the distortions the belief which has been withheld from the primary process, or - what is more frequent and more serious - it ends in the formation of protective delusions (megalomania) until the ego has been completely remodelled.

In his paper, "Further Remarks on the Neuro-Psychoses of Defence" (1896) he discussed a case of post-partum paranoid symptoms. Here again, self-accusations were defended against by being converted into accusations from the outside that the patient could deny. Once again this defense is described as requiring a secondary modification of the ego which accepts the reality of the projections. In his letter to Fliess of Novem-

ber 2, 1896, he notes the opposition to his theory of paranoia and then goes on to relate a dream from the night of his father's funeral, to which he had come late because he was in the barbershop. In the dream he was once again in the barbershop and saw a sign saying: You are requested to close an/the eye(s). He describes this dream as an outlet for a feeling of self-reproach. But now the reproach comes from outside, from the sign. The implication is that this dream provides support for his theory of paranoia.

In 1908, he described the essentially sado-masochistic nature of paranoid fantasies. At the end of "Instincts and their Vicissitudes," he noted the apparent transformation of affection into hostility (and of love into hate) which is so characteristic of paranoia.

Useful psychoanalytic ideas include recognizing the impact that early childhood experience can have on development and the way in which this can be exacerbated or ameliorated by one's relationship with caregivers. Freud saw projection as a key process in paranoia but whilst it is possible to identify projection in talk, for example in the kinds of explanation "by which the self attributes blame and criticism to others, while implausibly denying that blame and criticism attaches to itself" there is more debate about the functions this serves. Freud's original formulation was that it functioned to "ward off an idea that is incompatible with the ego, by projecting its substance into the external world", but the results of psychological research into so-called defensive attribution have been mixed . Of course, if defensive attribution served different functions for different people this might pose a challenge for group-based research studies. Drawing on the work of Auchincloss and Weiss (1992), Grosz (2013), argues that "paranoid fantasies ... protect us from a more disastrous emotional state – namely, the feeling that no-one is concerned about us, that noone cares".(Harper, 2022, p.7).

5.2 Social & Interpersonal Approaches

Socially-oriented theorists locate paranoia in a social and relational context. For example, Mirowsky and Ross's (1983) large community study found that paranoia was a

response to the negative operations of power in society:
« Social positions characterized by powerlessness and by the threat of victimization and exploitation tend to produce paranoia. Powerlessness leads to the belief that important outcomes in one's life are controlled by external forces and other persons, rather than by one's own choice and effort. This belief in external control interacts with the threat of victimization or exploitation to produce mistrust, which may then develop into paranoia»

Studies like this show the importance of attending to potential paranoia-generating societal processes. For example, paranoia is often widespread in totalitarian societies with centralized control and surveillance. In addition, in societies with high levels of inequalityand competitiveness it may be exacerbated when people are systematically victimized (e.g.on the basis of some characteristic like ethnic group etc.) romby and Harper (2009) argued that paranoia was a mode or tendency within subjectivity that was a response to structural locations of the kind that Mirowsky and Ross describe and of more proximal material influences like the kinds of living circumstances or the everyday experiences like discrimination associated with those structural locations. Melges and Freeman's (1975) cybernetic model of persecutory delusions similarly saw them as a response to the threat of a loss of control over the self or others, serving the function of predicting and counteracting control by others. These attempts then fed into interactional cycles which could, through feedback loops, exacerbate these fears. Kay et al (2009) reported that believing in conspiracy beliefs was one response to a perceived threat to personal control.

Another potential function of beliefs is that they can provide a person with a social role and "an identity not otherwise possible" . Believing in conspiracies canprovide people with an identity and community.(Harper,2022, p.p7-8)

5.3 The Hierarchy Model

The paranoia hierarchy is the widely cited model known in psychological literature (shown in figure 7.1). Freeman et al. (2005) developed a hierarchy of paranoia that organizes different paranoid thoughts, including less explicitly persecutory ideas, within a broad understanding of paranoia. This hierarchy ranks paranoid cognitions by the severity of perceived threat, starting with social evaluative concerns at the base (such as fears of rejection, vulnerability, or perceiving the world as dangerous), followed by ideas of reference, and culminating in persecutory thoughts. These persecutory thoughts are categorized from mild (e.g., people trying to irritate you), to moderate (e.g., people going out of their way to target you), to severe (e.g., people attempting to cause significant harm). Other theoretical models of paranoid cognition generally focus on persecutory beliefs in isolation, examining their origins and maintenance. Additionally, schizotypy theories describe 'suspicious' personality traits associated with a higher incidence of paranoid thoughts.

Figure 7.1. The Paranoia Hierarchy
(Nivetha et al., 2023, p.383)

As indicate in figure 7.1: the most common type of suspiciousness is that of a social anxiety or interpersonal worry theme; ideas of reference build upon these sensitivities; persecutory thoughts are closely associated with the attributions of significance; as the severity of the threatened harm increases,the less common the thought; and suspiciousness involving severe harm and organisations and conspiracy is at the top organisations and conspiracy is at the top of the hierarchy. The implication is that severe paranoia may build upon common emotional concerns, consistent with a recent cognitive model of persecutory delusions.

5.4 Threat Perception & The Attributional Model

The perception of threat is a central feature of paranoia almost by definition.According to Moutoussis et al.(2007), several studies have examined this by asking paranoid pa-

tients to estimate how often they experienced positive, negative, and neutral events in the past, as well as the likelihood of these events occurring in the future. These studies show that patients report high frequencies for both past and future negative events, which can be broken down into three components. First, there is substantial evidence that paranoid patients have experienced unusually high levels of adverse events, such as discrimination and victimization. This not only affects their evaluations of past events but also inflates their predictions of future negative events due to reliance on past recollections. Second, patients tend to recall threat-related information more readily, further biasing their future estimates through the availability heuristic. Third, even after accounting for these factors and comorbid anxiety and depression, paranoid patients still overestimate future negative events. This suggests a specific abnormality in the mechanism for processing negative experiences, significantly contributing to the development of paranoid delusions.

Paranoid patients tend to exaggerate perceived and potential negative outcomes, prompting questions about appropriate cognitive responses. When faced with significant events, people universally seek explanations, a process studied by attribution theory. Attributional models of psychopathology suggest two main explanations for negative events: internal (self-blame) and external (blaming others or circumstances). Most people favor external attributions to protect self-esteem, a phenomenon known as the self-serving bias.

The types of attributions people make significantly affect their psychological health. Many studies indicate that depressed individuals often attribute negative events internally. In contrast, paranoid individuals tend to blame external factors, particularly personal ones. These findings have inspired theories linking attributional processes to paranoid delusions. An early model suggests that paranoid patients possess negative self-schemas, which activate discrepancies between their ideal self and actual self-perception. To avoid these discrepancies, they attribute the cause to external personal

factors (other people's actions), leading to the belief that others have hostile intentions. This model posits that persecutory delusions develop from the repeated use of this defensive mechanism in response to ongoing threats.

5.5 Paranoia & The Theory Of Mind

Gallese proposed that the capacity to understand others as intentional agents could well be a basic organizational feature of our brain, enabling our rich and diversified intersubjective experiences. This perspective could be in a position to offer a global approach to the understanding of the vulnerability to major psychoses such as schizophrenia. On this note, the theory of mind (ToM) refers to the capacity of attributing mental states such as intentions, knowledge, beliefs, thinking and willing to oneself as well as to others. Amongst other things, this capacity allows us to predict the behavior of others.

The ToM also includes the knowledge that the beliefs and desires of others may differ from our own. Central tenets of the ToM are beliefs, desires and actions. Together with our own beliefs and desires, our mental picture of reality leads us to decide on this or that course of action. However, the mental picture does not always correspond to actual reality. Meanwhile, there are now several fMRI studies which support the cortical correlates of the ToM. Frith postulated that paranoid syndromes exhibit a specific ToM deficit, e.g. delusions of reference can be explained, at least in good part, by the patients' inability to put themselves in another person's place and thus correctly assess their behavior and intentions. Thought insertion and ideations of control by others can be traced back to dysfunctional monitoring of one's own intentions and actions. Hence, thoughts enter the patient's consciousness without his or her awareness of any intention to initiate these thoughts. The inability of these patients to correct errors is also believed to rest on an internal monitoring disorder.

However, the question remains whether delusional ideas in a narrow sense and symptoms like thought insertion or other positive symptoms of schizophrenia should be

discussed under the same perspective. Seen from this angle, serious neurophenomenological arguments against the global theory of meta-representational self-monitoring processing deficits in schizophrenic patients emerged . Nevertheless, Frith and Frith found a particularly strong correlation of the medial and the lateral inferior prefrontal cortex and the temporal parietal transition brain regions with delusions and ToM deficits. Since deluded patients in symptomatic remission performed as well as normal controls at ToM tasks, ToM deficits seem to be a state rather than a trait variable . Furthermore, the specificity of ToM deficits in delusions is also questionable because delusional patients may perform normally at ToM tasks. Nevertheless, it is currently held that the medial prefrontal cortex is important for the perception of self whereas the lateral frontal inferior cortex plays an important role – via mirror neurons – in planning and carrying out actions . Psychological processes, on the other hand, are usually based on observations of the behavior of others, and seem to be connected with the superior temporal sulcus. Another part of the 'social brain' circuitry which may be relevant in the context of ToM is the amygdala. Recent work by Shaw et al. suggests that lesions to the amygdala interfere with ToM reasoning most consistently if they were acquired relative early in life. This agrees with developmental theories of schizophrenia but the etiological relevance of ToM in delusional disorders is yet to be determined.(Kunert et al,2007,p.197)

6 Therapeutic Approach To Delusional Disorder

6.1 Cognitive Therapy

Cognitive therapy also has interesting applications for the treatment of paranoid patients. The central assumption of this approach is that personality disorders are associated with deeply ingrained, maladaptive beliefs . In the case of paranoid personality, these include thoughts such as "people cannot be trusted" and "if I get close to people, they will find

out my weaknesses and hurt me." The therapist works with the client to identify and recognize these cognitive distortions and their influence on the person's behavior. The paranoid person is encouraged to test the validity of these maladaptive thoughts. Over time, the goal is to help the person learn to replace them with more adaptive thoughts are more accurate attributions.

As treatment progresses, emphasis should shift to modifying their belief system regarding the self and others. Many of the techniques that are used during this phase of treatment are borrowed from cognitive therapy (CT) and schema therapy, a type of cognitive therapy that was developed specifically for treating PDs. The central assumption of cognitive therapy is that personality disorders are associated with deeply ingrained, maladaptive beliefs that are often inaccurate.Therefore, the goal of CT is to replace their maladaptive beliefs with those that are more "adaptive" and "accurate." As these thoughts are intrinsic to the personality-disordered individual, it is hard, if not impossible, for them to recognize and acknowledge that their core beliefs need to be changed. With the help of the therapist, clients are encouraged to identify and recognize cognitive distortions and their influence on behavior.

Once the maladaptive schemas have been identified, the client is encouraged to test the validity of these maladaptive thoughts. Examining evidence for and against the schemas of mistrust and abuse that are predominantly found in those with paranoid PD, may be achieved by having a series of structured dialogues between the client and the therapist in which both parties try to constructively argue for and against the schema . Such a method allows the patient to systematically confront and challenge his or her maladaptive schemas.

In the process of challenging and changing their maladaptive schemas, clinicians should encourage patients to think about how their behavior may have elicited certain reactions from others. Paranoid individuals have learned to be hypersensitive to the judgments of others, and as a result, they behave in ways that invite the type of reac-

tion they anticipate and fear. As they react in hostile manners that drive people away, paranoid individuals become convinced that their suspicions were correct. In order to break the cycle, clients should be taught how to be less sensitive to criticism and how to act in ways that will not invite attack or avoidance . The latter is achieved by utilizing social skills training techniques such as instructional role-playing, behavior rehearsal, and videotaped feedback, through which they are taught to attend to more appropriate social stimuli, to interpret information more accurately and to receive feedback from others in a non-defensive way.(Oltmanns & Okada,2006 ,p.p510-511)

Conclusion

The neurobiological foundations, particularly the roles of neurochemical and biological implications, offer a fundamental explanation of the mechanisms underlying schizophrenia and delusional disorders. Although they cannot completely predict all risk factors, this framework provides essential information for research and treatment, guiding therapeutic approaches across age groups and cultural contexts. Its continued relevance underscores the importance of advancing our understanding of these disorders in clinical practice.

Unit 5: Depressive Disorders

Depression

Objectives

- Identify the etiology of major depressive disorder.
- Review the appropriate management of major depressive disorder.
- Outline the typical presentation of a patient with major depressive disorder.

Introduction

Although depression is among the most common of all mental health disorders, the nature of depression remains controversial and difficult to define.Depression is thought to occure in a number of subtypes,which includes major depressive disorder,persistent depressive disorder,adjustment disorder with depression,bipolar depression,seasonalaffective depression,premenstrual dysphoric disorder, bereavement,grieving,etc.Further complicating our understanding of depression is that studies related to the topic of « depression »may not define the manner in which this ter mis being used.The term depression is often used interchangeably with what would be more precisely be termed depressive disorders,depressive symptoms,or depressed mood.Depression is also used as a susstitute for major depressive disorder or one of the other unipolar mood disorder with specific diagnostic criteria.(Hegmann,2020,p.8)

The lecture explores various facets of depression, beginning with its definition and historical background, and then delving into its biological causes and some theoretical perspectives on the topic.

1 Definition & Delimitation

The word depression comes from the Latin “depressio” which means sinking. The person feels sunk with a weight on their existence. It is a mood disorder that varies from: normal transient low mood in daily life itself, to clinical syndrome, with severe and significant duration and associated signs and symptoms, markedly different from normality.

Depression consists of a disease with decayed mood as its main symptomatology. There are also painful feelings, bad humor, anguish and panic attacks, performance decay of various psychic and cognitive functions, tendency to isolation, demotivation, apathy, abulia, difficulty to enjoy, hopelessness, motor inhibition, hypotonia and negative thoughts, including possible delusions in cases of serious severity. On the other hand, it can present a very diverse associated somatic symptomatology, some organic alterations often corresponding to larval or encapsulated ways of going through a depression. It is considered a mental disease consisting of a mood disorder, being its usual symptom a state of dejection and unhappiness that may be transient or permanent. In this sense, it is defined as a mental disorder characterized by the presence of sadness, loss of pleasure, feelings of guilt and low self-esteem, accompanied with alterations in the sleep pattern and the appetite, lack of concentration, and feelings of being tired, which can become chronic and recurrent, making the person dysfunctional in their daily activities; when it is mild it can be treated with psychotherapy, but when it is moderate or severe, pharmacological treatment may be needed.

Depression therefore is conceived at the same time as a “mental disorder”and as a “mood disorder”, although both perspectives coincide in a psychological disorder conception. In addition, it is also emphasized that “it can persist in time, until it makes dysfunctional the one who suffers from it”.

Vallejo, indicates that the term depression is used in three different ways: symptom,

syndrome and disease. As a symptom, it can accompany other psychic disorders, such as anguish disorders; as a syndrome, it groups processes characterized by sadness, inhibition, guilt, disability and loss of vital impulse, and as a disease, it is outlined as a disorder of biological origin in which an etiology, a clinic, a course, a prognosis and a specific treatment can be established. From the previous perspective, it seems that depression, if considered a "disease" only to emphasize an organic etiology, could lose both the entity of "disorder" and of "symptom", in contrast to understanding the human being as a biopsychosocial entity and the tripartite biological, psychological and social composition of all alterations that could possibly affect it.(Rondón Bernard,2018, p.6)

2 History

- **Ancient Times:** Depression, referred to as "melancholia" by Hippocrates, was believed to result from an imbalance of bodily fluids, particularly an excess of black bile.
- **Middle Ages:** It was often viewed through a religious lens, associated with sin or demonic possession, and treated with prayer or exorcism.
- **Renaissance to 19th Century:** The understanding of mental health began to evolve, with philosophers like Descartes and Locke considering the mind's role in depression. This period saw the beginnings of more humane treatment approaches.
- **19th Century:** Psychiatry emerged as a medical specialty, with Freud's psychoanalytic theory emphasizing the unconscious mind and childhood experiences as contributing factors.
- **20th Century:** Advances in understanding the biological basis of depression led to the discovery of neurotransmitters. The introduction of treatments like elec-

troconvulsive therapy (ECT) and psychotropic medications marked significant progress. The DSM-III standardized diagnostic criteria in 1980, improving the understanding of various depression subtypes.

- **21st Century:** Today, depression is recognized as a complex disorder influenced by biological, psychological, and social factors, with ongoing research into effective treatment modalities, including psychotherapy and pharmacotherapy.

3 Clinical Symptoms

The symptoms of depression can be divided into emotional and physical. The emotional symptoms of depression are stress, sadness, loss of interest, anxiety, hopelessness, difficulties with concentration, feeling of guilt, and suicidal thoughts. Physical symptoms include lack of energy, fatigue, pain, sleep disturbances, headaches, and psychomotor activity changes. The complexity of depression is evidenced by the classification of this illness proposed by the (American Psychiatric Association (APA), 2013) shown in Figure 8.1.(Stachowicz & Sowa-Kućma, 2022, p.2)

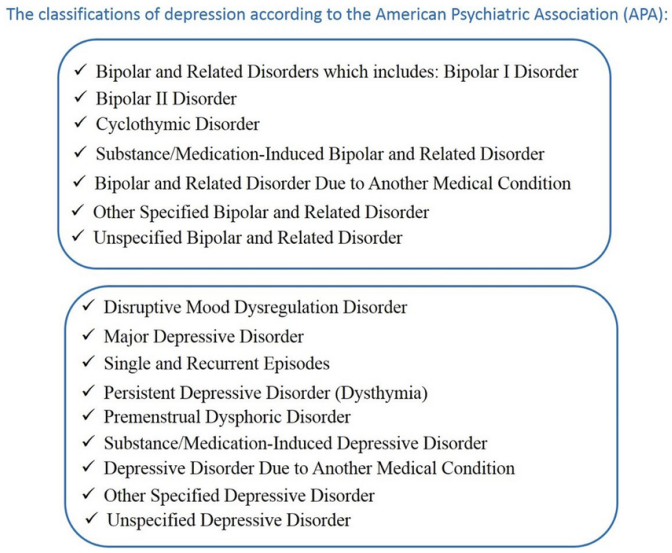


Figure 8.1. The classification of depression
(According to APA)

4 The Different Types Of Depression

4.1 Major Depressive Disorder (MDD)

MDD is a specific clinical diagnosis with clusters of symptoms including prolonged depressed mood for more than two weeks, diminished interests, significant weight loss, loss of energy.(Mengxin Cai,2023,p.270)

4.2 Persistent Depressive Disorder (PDD)

PDD Was a new diagnosis in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) in 2013 that combined dysthymia and chronic major depressive disorder. The classification of depressive symptoms has a complicated history dating back to the description of melancholic temperament by Hippocrates. According to the DSM-5, persistent depressive disorder is characterized by a depressed mood that occurs for most of the day, for more days than not, for at least 2 years, or at least 1 year for

children and adolescents. Major depression may precede PDD, and major depressive episodes may occur during PDD, which is known as double depression.PDD may begin early in life, and depressive symptoms may wax and wane but never fully resolve.(Patel & Aslam, 2024)

Dysthymia, literally meaning 'being of bad mood' or 'ill-humor' is an illness characterized by a number of affective, neurovegetative and cognitive symptoms. The diagnosis of dysthymic disorder was introduced in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) to characterize chronic depression of 2 or more years and to encompass disorders which had previously been considered characterologically based, including neurotic depression, chronic minor depression, and characterological depression.While the severity of dysthymia is usually less profound than that of acute major depressive disorder, symptoms may fluctuate in intensity. Furthermore, several subtypes of dysthymia have been proposed based on specific symptoms, family history, and age of onset; subaffective dysthymia is thought to be of biological origin, while character spectrum dysthymia is more personality-based.Currently, DSMIV stipulates that a diagnosis of dysthymia includes depressed mood, coupled with two or more of the following: poor appetite or overeating, insomnia or hypersomnia, low energy/fatigue, low self-esteem, poor concentration or difficulty making decisions, and feelings of hopelessness.Dysthymia also frequently has an early and insidious onset, and is associated with pathology of character, albeit these may not play an etiological role.(Griffiths et al.,2000,p.243)

4.3 Bipolar Depression

(Hypomanic Episode) is the second episode in Bipolar disorder which is an affective disorder that results in chronic repeated severe mood changes with manic and depressive episodes; it is associated with characteristic cognitive, physical, and behavioral impairments .Depression in patients with bipolar disorder is associated with long-term

morbidity and impaired function.(Tokumitsu K,2021,p.2). The clinical features of bipolar depression are illustrated by Robert M. Post (2005) in figure 8.2.

Affective	Cognitive	Physical	Chemical	Brain Alterations
Sadness	Poor self-esteem	Change in sleep	Hypercortisolism	Selective decrease in neurons or glia in prefrontal and anterior cingulate cortex and in amygdala
Apathy	Poor concentration	Change in appetite	Decreased somatostatin in CSF	Decreases in neuronal NAA in frontal cortex
Anhedonia	Indecisiveness	Decreased activity	Decreased intracellular calcium in blood elements	Decrease in prefrontal GFAP
Irritability	Suicidal ideas	Low energy		Decreases in reelin and GAD67
Anxiety	Self-blame	Change in weight		Frontal and hippocampal hypofunction on PET
				Amygdala and cerebellar hyperactivity on PET
				Loss of normal balance in positive and negative connectivity among brain regions

Figure 8.2. The clinical features of bipolar depression
Robert M. Post (2005)

Other forms of depression: There are also fewer common forms of depression, such as postnatal depression , a form of depression that occurs after the birth of a child, seasonal depression, a type of depression that occurs primarily during a particular season, etc. These forms of depression can be linked to certain hormones, such as in the case of postnatal depression, or to the perception of light, as in the case of seasonal depression.(Bourin,2020)

5 Differential Diagnosis

According to DSM 5, MDD is demarcated from normal sadness or bereavement; however, in patients who are mourning who develop symptoms severe enough and persistent beyond the acute grieving period, an MDD diagnosis can be given. While it is possible to diagnose MDD based on a single depressive episode, MDD is recurrent in the majority of cases.

The key differential diagnosis of MDD is with bipolar depression and with persistent depressive disorder. The differential diagnosis of MDD from bipolar depression rests entirely with the presence of a history of hypomania or mania, which is characterized by a clear period of elevated mood or irritability and with at least three of the

following symptoms presently overtly: inflated self-esteem, reduced need for sleep, increased speech, flight of ideas, distractibility, increased activity in goal-directed tasks, and involvement in risky behavior.

Persistent depressive disorder is a chronic disorder and describes patients who have been depressed for >2 years. Apart from depressed mood, only two of six symptoms (appetite disturbance, sleep disturbance, loss of energy, decreased self-esteem, poor concentration, or hopelessness) are required for the diagnosis. Thus, it is possible to meet criteria for persistent depressive disorder without having MDD. If a patient meets criteria for MDD, then the patient would receive two diagnoses — MDD and persistent depressive disorder(Otte et al.,2016,pp. 18-19)

6 Aetiology of Depression

6.1 Pathophysiology of Depression

- **Serotonin alterations in depression**

  Serotonin (5- HT; 5-hydroxytryptamine) occurs naturally in the body. In the periphery, serotonin acts both as a gastrointestinal regulating agent and a modulator of blood vessel tone. Only 2% of the body's serotonin is found in the brain as a neurotransmitter. As a neurotransmitter, serotonin is involved in the modulation of motor function, pain perception, appetite and outflow from the sympathetic nervous system. Historically, Hippocrates was the first to describe melancholia (depression) as a condition associated with "aversion to food, despondency, sleeplessness, irritability and restlessness. (Saldanha et al., 2009)

  There is increasing evidence that alterations in the brain serotonergic system are involved in the pathophysiology of depression. It has been suggested that 5-HT receptor dysfunction might contribute significantly to the development of depres-

sion. 5-HT receptors are highly expressed in the human limbic system, including the amygdala, hippocampus, thalamus, putamen, anterior cingulate cortex and midbrain. Among the 5-HT receptor types (5-HT1A, 5-HT1B, 5- HT2A, and 5-HT4), 5-HT1A has generated much research interest because of its involvement in recognition, learning memory, and hippocampal neurogenesis, as well as its response to antidepressant treatment . Furthermore, 5-HT1A dysfunction often accompanies depression. (Wang et al., 2016, p.1)

- **Norepinephrine alterations in depression**
  Several lines of evidence suggest that Norepinephrine NE is a neurotransmitter of major importance in the pathophysiology and treatment of depressive disorders.
  - NE projections from the locus coeruleus innervate the limbic system, which is implicated in the regulation of emotions. Numerous differences have been found in elements of the NE system in postmortem brains from depressed patients and healthy controls.
  - Genetic studies show that mice with genetically engineered functional enhancement of the NE system are protected from stress-induced depression-like behaviors.
  - Experimental depletion of NE in the brain results in a return of depressive symptoms after successful treatment with NE antidepressant drugs.
  - Therapeutic agents which specifically increase NE activity are effective antidepressants.

Noradrenergic pathways in the brain arise from the cell bodies in the locus coeruleus and project to different cerebral regions and to the spinal cord (Figure 8.3) . In addition to major projections to the frontal cortex, NE neurons project to the limbic system, whose various components such as the amygdala, hippocampus, and hypothalamus are implicated in emotion and cognition as well as a number of functions modified in depressed patients such as appetite, response to pain, levels of pleasure, sexual satisfaction, and aggressive behavior.(Moret and Briley,2011,p.10)

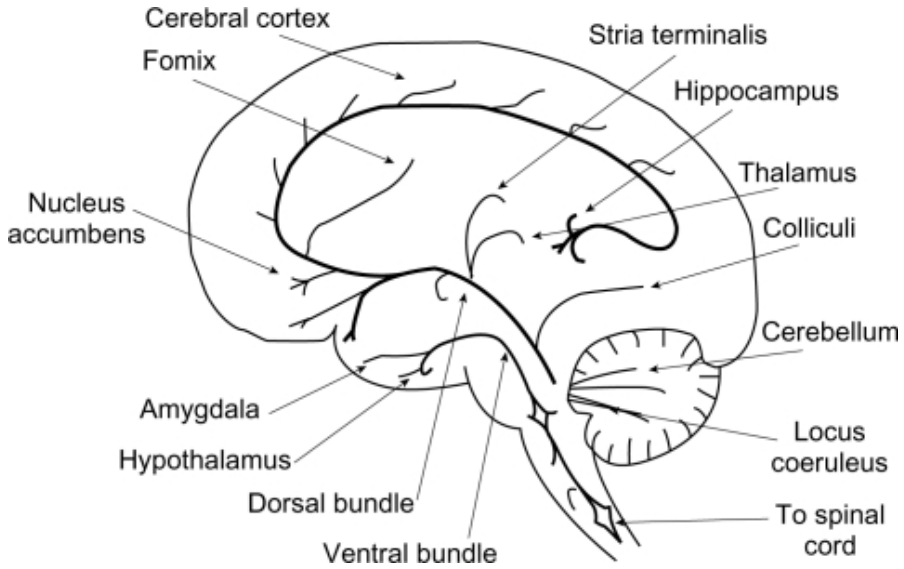


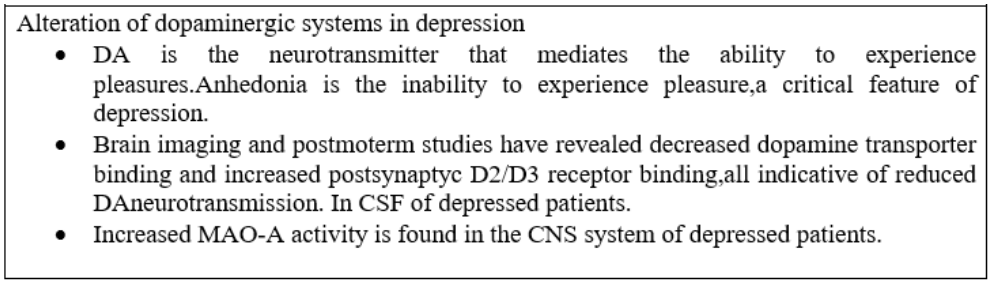
Figure 8.3. Sagital section of the human brain showing the principal noradrenergic pathways (Moret and Briley,2011,p.10)

- **Dopamine alterations in depression**

  Motivation, psychomotor speed, concentration, and the ability to experience pleasure are all linked in that they are regulated in part by dopamine (DA)– containing circuits in the central nervous system and impairment of these functions are prominent features of depression.(Dunlop & Nemeroff ,2007,p.327) . The four major dopaminergic pathways are i) nigrostriatal pathway running from substantia nigra to the dorsal striatum (i.e. caudate nucleus and putamen), ii) mesolimbic

pathway from ventral tegmental area (VTA) to the ventral striatum (i.e. nucleus accumbens), iii) mesocortical pathway from VTA to prefrontal and cingulate cortex, and iv) tuberoinfundibular pathway from hypothalamus to pituitary gland. (Malén et al., 2023).

The emergence of a DA hypothesis of depression is not surprising in view of the fact that the inability to experience pleasure, anhedonia, is considered by many to be the most important pathognomonic symptom of depression, and pleasure, whether associated with eating, social, or sexual behavior, is primarily mediated by activation of DA neurons. The box in the figure 8.4 summarizes the evidence for the role of altered dopaminergic circuits in depression. Both postmortem tissue and PET imaging studies have revealed reduced DA transporter binding sites and increased postsynaptic DA D2/D3 receptor density, indicative of a reduction in the synaptic availability of DA in depression.(Saveanu & Nemeroff,2012 ,p.54)


Alteration of dopaminergic systems in depression

- DA is the neurotransmitter that mediates the ability to experience pleasures.Anhedonia is the inability to experience pleasure,a critical feature of depression.
- Brain imaging and postmoterm studies have revealed decreased dopamine transporter binding and increased postsynaptyc D2/D3 receptor binding,all indicative of reduced DAneurotransmission. In CSF of depressed patients.
- Increased MAO-A activity is found in the CNS system of depressed patients.

Figure 8.4. The evidence for the role of altered dopaminergic circuits in depression (Saveanu & Nemeroff,2012 ,p.54)

As mentioned in Tamura et al.(2022),recent neuroimaging studies have provided evidence for dopamine dysfunction in depression by examining the dopamine transporter (DAT). DAT, a plasma membrane protein found specifically in dopaminergic neurons, is crucial for regulating dopamine at the synapse. Imaging studies show that DAT binding indicates both the number of presynaptic dopaminergic

neurons and the presence of DAT at presynaptic terminals. Multiple studies have linked major depressive disorder (MDD) to decreased DAT binding in the midbrain and striatum, though findings for bipolar depression have been inconsistent. This reduction in DAT binding may be due to the downregulation of DAT as a result of chronic dopamine depletion, suggesting a potential underlying mechanism for depression.

Stahl has suggested that it can be instructive to consider brain neuroanatomy in terms of specific functional centers (figure 8.5). The "emotional" and "somatic" centers in the brain receive projections from both NE and 5-HT as well as DA pathways. The "cognitive" centers, on the other hand, receive input only from NE as well as DA and histaminergic projections, but not 5-HT projections.
The figure 8.5 summarize the different brain centers

Emotional centers
NE projections from the locus coeruleus to the hypothalamus
NE projections from the locus coeruleus to the amygdala and prefrontal cortex
5-HT projections from the midbrain raphe to the hypothalamus
5-HT projections from the midbrain raphe to the amygdala and prefrontal cortex
DA projections from the ventral tegmentum to the nucleus accumbens
Somatic centers
NE projections from the locus coeruleus to the hypothalamus
NE projections from the locus coeruleus to the cerebellum
NE projections from the locus coeruleus to the spinal cord
5-HT projections from the midbrain raphe to the hypothalamus
5-HT projections from the midbrain raphe to the striatum
5-HT projections from the midbrain raphe to the spinal cord
DA projections from the substantia nigra to the striatum
Cognitive centers
NE projections from the locus coeruleus to the dorsolateral prefrontal cortex
DA projections from the ventral tegmentum to the dorsolateral prefrontal cortex
Histamine projections from the hypothalamus to the dorsolateral prefrontal cortex

Figure 8.5. Neuronal projections to different brain "centers"
(Moret and Briley,2011,p.11)

Executive function is a complex organization of higher mental functions that process mental and environmental input to enable efficient problem-solving capacity in a way that is acceptable to both the individual and society. It includes inhibition of irrelevant or unacceptable behavior, the suppression of nonpertinent information, the regulation of verbal and nonverbal working memory, self-regulation of affect, motivation and arousal, planning, decision-making, self-monitoring of the problem-solving process, and self-evaluation of the results of the action taken. Anatomically, this occurs in the prefrontal lobe of the cortex and its afferent and

efferent structures involving the neurotransmitters NE and DA and to a lesser degree acetylcholine and 5-HT. Executive function is also fundamental to social relationships. Social dysfunction in depression is possibly one of the most important factors affecting the quality of life of patients. Considerable clinical data suggest the importance of NE in the improvement of clinical dysfunction in depression.

6.2 The Neuroanatomy of Depression

Although there is little doubt that various neurotransmitter systems are pathologically involved in depression, no single neurotransmitter system seems to be solely responsible. This is not surprising when one considers the panoply of symptoms that comprise the depressive syndrome, including depressed mood, loss of interest in usual activities, inability to experience pleasure, impaired concentration, disturbed sleep, decreased appetite, and suicidality. A more recent conceptual approach to the biology of depression is to consider it a disorder involving several critical brain regions and associated pathways.

Advances in brain imaging have allowed the identification of these brain regions and associated circuits. Structural brain imaging using magnetic resonance imaging has revealed altered volumes of several brain regions in patients with depression, most notably a reduction in hippocampal and caudate nucleus size and an increase in pituitary volume. It is now evident that some of the previously described changes in certain brain structures may be more likely caused by early life stress during a critical period in brain development than to depression perse. PET studies led by Mayberg and colleagues and Drevets support the hypothesis that depression is characterized by abnormalities in limbic system– cerebrocortical circuits, more specifically, reduced activity in frontal cortical areas and hyperactivity in the amygdala and other limbic sites. The subgenual cingulate cortex (Cg25) seems of paramount importance; this brain area

shows a striking decrease in activity in response to clinical improvement of depression after treatment with SSRIs, electro-convulsive therapy and other novel treatments and is a target for deep brain stimulation treatment of refractory depression.(Saveanu & Nemeroff,2012,p.55)

6.3 Inflammatory Theory

Research studies conducted within the last ten years have confirmed that both physical and psychological (emotional) stress increases the likelihood of occurrence of mental disorders (including depressive disorders) owing to the action of a series of hormonal and biochemical mechanisms , as well as epigenetic mechanisms, which has been recently confirmed.

6.3.1 The kynurenine Pathway

Hyperactivity of the hypothalamic-pituitary-adrenal axis (HPA) and dysregulation of the immune system are the source of irregularities in the activity of the kynurenine pathway. Its basic role in a healthy organism is to transform tryptophan into two essential compounds engaged in mood regulation, i.e., serotonin and melatonin . Based on the kynurenine pathway hypothesis of depression etiology, inflammatory factors cause excessive activation of indoleamine-2,3-dioxygenase (IDO), an enzyme present in microglia, astrocytes and neurons . This enzyme catabolizes tryptophan, the source of serotonin, into kynurenine (KYN), a neurotoxic substrate which increases the risk of neurodegenerative and neurotoxic processes. In this way, IDO reduces the amount of tryptophan available for the production of serotonin , which is directly linked with the etiology of depression.

6.3.2 Inflammatory Markers in Depression

Enzymes of inflammation : Manganese superoxide dismutase (MnSOD), myeloperoxidase (MPO), and inducible nitric oxide synthase (iNOS) are among the enzymes of inflammation which take part in the etiology of recurrent depressive disorders (RDD) . Not only do the compounds take part in an inflammatory reaction, but they are also actively engaged in the production of free radicals, as well as damage proteins, fatty acids and cellular DNA. This leads to brain damage both through neurogenesis deterioration as well as intensification of neurodegenerative processes .(Gałecki & Talarowska,2018, pp.438–439)

Piotr Gałecki and Monika Talarowska(2018), along with other researchers, have provided evidence of genetic and biochemical factors associated with recurrent depressive disorders (RDD). Gałecki and colleagues found that manganese superoxide dismutase gene polymorphisms (Ala-9Val and Ile-58Thr) are linked to depressive symptoms in RDD patients. Madrigal et al, showed that stress increases iNOS expression in the hippocampus and cerebral cortex, a finding echoed by Gałecki et al, who observed elevated iNOS expression at the mRNA level in RDD individuals. Kim et al, discovered that RDD patients who had attempted suicide had significantly higher nitric oxide (NO) levels compared to those who had not and to healthy controls. Furthermore, Gałecki et al. reported increased MPO expression at the mRNA level in RDD patients and identified a higher prevalence of the G-463G genotype and -463G allele in these patients, indicating a genetic predisposition to depression.

6.4 Psychological Theories

6.4.1 Psychoanalytic Theory & Depression

Freud began his wellknown exploration of depression and its link to aggression in “Mourning and Melancholia” (1917). He conceptualized that in response to the ex-

perience of a loss, the individual internalizes the lost object as a way of holding on to it. The outcome of maintaining the loss is twofold: it helps to ease the grieving, and it provides an alternative target for hostility toward the lost object.

Several years later, in Civilization and Its Discontents, Freud (1930) expanded on these views in the context of family and society. According to Freud, as the result of an internal set of standards and values by which one judges him- or herself (i.e., a superego), individuals may unconsciously inhibit their hostility or aggression to avoid the negative consequences of expressing it externally; thus they preserve their place in the family or, on a larger scale, society. This process results in internalized hostility that predisposes a person to depressive symptoms. Freud proposed that the link between depression and internally directed aggression is mediated by the superego and is due, in part, both to one's expectation of aggression (derived from unique perceptions of one's parents) and to one's own innate level of aggressiveness. "What it amounts to is that, in the formation of the superego, and the emergence of a conscience, innate constitutional factors and influences from the real environment act in combination".

Further psychoanalytic views of depression—Freud's view of depression and its link to aggression has been elaborated and modified by numerous theorists. Abraham's critical contributions to the theory of depression (1911), though provisional, actually preceded "Morning and Melancholia" (Freud 1917). Abraham viewed depressed individuals as having suffered an enormous frustration at the hands of a loved one and therefore unconsciously longing to destroy the object of affection. This perspective served as a foundation for later theorists who proposed that the intense love and hate for the same object resulted in guilt, leading to self-reproach, the need for punishment, an obligation to protect the loved one from the destructive impulses, and, finally, tormenting depression.

In Bibring's model of depression (1953), depressive symptoms result from frustrated aspirations and the experience of helplessness. An individual's incapacity to fulfill his or

her wishes to be loved, loving, secure, and good, rather than unworthy of love, insecure, aggressive, and destructive, leads, according to Bibring, to depression. In Bowlby's view (1960), separation from the mother induces powerful and intolerable hate in the child. This unmanageable and unacceptable hate is pushed down and displaced onto others and the self.

Building on Freud's early sensitivity to the developmental origins of depression, Blatt (1974) differentiated between "anaclitic" and "introjective" depression. Anaclitic depression is characterized by an intense longing for closeness and a complementary fear of abandonment. Introjective, or self-critical, depression is markedly different in that the pain is related to powerful guilt, inferiority, a sense of worthlessness, and internally directed aggression.

More recently, Brenner (1991) and Milrod (1988) have offered somewhat contrasting contemporary views of depression. Brenner's theory rests on the notion that depression is an affect or personality trait that is present in all individuals. He theorizes that depressive symptoms speak to the structure of defenses and affect regulation, rather than to the etiology or origins of the conflict. In fact, he argues that internally directed aggression is not the cause of depression but rather a possible defensive response, as are depressive symptoms, to depressive affect. In stark contrast, Milrod argues that depression is not an affect but a mood, or temporary ego state. According to Milrod, depressive symptoms are not defenses; rather, he proposes that all depressive symptoms result from anger directed toward the self in consequence of loss. (Haddad et al, 2008, p.p3-4)

6.4.2 Cognitive Behavioral Theory & Depression

Cognitive behavioral approaches vary in their perspectives on fundamental thoughts and their proposed role in the development of depression.

Beck's view of psychopathology

Beck identifies faulty information processing as a cause of psychopathology and implies that humans can be understood by the cognitive processing constructs they build. Throughout development, biased perceptions in form of stimuli, ideas, experiences and beliefs are stored accumulatively as part of these cognitive processing structures called schemas.

The inference of meaning is influenced by the idiosyncratic schemas the person has established. Since cognitive constructs are subjective and established by the individual's experiences and interpretations thereof, such meaning generation may be highly unrealistic, since it is very difficult to verify their authenticity against reality. If the meaning generation process, influenced by such maladaptive schemas, deviates significantly from reality, cognitive distortions and emotional disorders follow .More specifically, schemas influence the appraisal mechanismthat is responsible for the affective response based on the individual's appraisal of an external event. Emotional disorders are characterized by appraisal and subsequent emotional reactions that are incongruent to the individual's external reality . Beck extended his initial theoretical model by incorporating the concept of schema activation. Schemas are strengthened by repeated and potent life events especially when such events are adverse and stressful. Strengthened schemas are easily activated and take control over the information processing system. If dysfunctional or maladaptive schemas become activated the probability of the individual experiencing psychopathological symptomatology is increased.

As a part of the cognitive model, representations of abstract schema content exist in the form of beliefs. As such, beliefs contain assumptions, expectancies, fears, rules, and evaluations. Clark et al. (1999) differentiate a hierarchy of beliefs according to three levels of cognition. Core beliefs represent the inner most level of beliefs, tend to be absolutistic, and contain underling views about ourselves, others and the world. Intermediary beliefs reside at a higher level in consciousness and influence a person's view of a situation, ultimately affecting thinking, affect and behavior. Automatic thoughts

are viewed as a derivative of beliefs influenced by core and intermediary beliefs . As such, automatic thoughts tend to be specific, discrete and occur in "telegraphic style" alongside the mainstream of thought. Automatic thoughts occur in an autonomous manner, are difficult to suppress, and are idiosyncratic among other individuals with similar psychopathology. Clark and Beck (2011) summarized this specificity, that content and orientation of automatic thoughts and processing bias differ between the disorders, as part of the content specificity hypothesis.

Ellis' View of Psychopathology

Ellis views cognition as the "most important proximal determinant of human emotion". Emotional distress is caused by dysfunctional thought processes, which include exaggeration, overgeneralization, oversimplification, and faulty or untested assumptions. Central to REBT theory is the ABC model, which states that an activating event (A) causes emotional, behavioral, and cognitive consequences (C), a process that is mediated by the person's rational or irrational beliefs (B). Rational beliefs can be distinguished from irrational beliefs by the fact that they cause functional and healthy consequences, which are flexible, logical, and foster goal achievement. Irrational beliefs, on the other hand, are non-pragmatic, rigid, not consistent with reality, and lead to emotional disturbance . These rigid beliefs, as part of rigid demanding core schemas, lead to extreme beliefs and subsequently to distorted inferences about external reality. Thus, REBT views cognitive rigidity as the root cause of emotional and psychological disturbance.

REBT distinguishes between three levels of cognitions; the first level of cognition is related to surface cognitions that can be easily accessed and tested against reality. First level cognitions are related to inference generation that can be faulty and are related to automatic thoughts . Second level cognitions are evaluative cognitions, which appraise the "badness" of the inferences of the first level cognitions and include the individual's

evaluation of coping resources and ability to tolerate the inference. Third level cognitions, according to REBT, involve central imperative demands, which are schematic representations of how the individual wants the world to be. Imperative demands refer to the rigid adherence to an unrealistic and absolute expectation of the world, the self, and other individuals. People construct their representation of reality in the form of schemas. If individuals perceive an inconsistency of incoming information that conflict with their expectations of the world, emotional arousal occurs, causing assimilative or accommodative efforts to resolve this discrepancy. Demandingness (DEM), so REBT postulates, is indicative that the person perseverates assimilative efforts to cope with schema discrepant information, resulting in continued arousal and perception of threat.

According to REBT theory, demandingness leads to second level irrational beliefs that are evaluative in nature. REBT distinguishes between the second-level irrational beliefs awfulizing (AWF), frustration intolerance (FI) and global evaluation of worth such as self/others/world-downing (SD). Awfulizing is characterized by exaggerated negative thoughts about self, others, or the world, often represented by language such as “terrible, awful, or catastrophic” . Awfulizing represents beliefs that something is awful or catastrophic and as such represent extreme evaluations that stem from absolutistic beliefs. Frustration Intolerance refers to the irrational belief that one can’t stand and endure the activating event and contains the belief that happiness could not exist if a specific situation were to occur. Frustration Intolerance is related to one’s appraisal of one’s strength and effort that can be mustered despite pain, discomfort and threat. Global evaluation of worth refers to the absolutistic evaluation of human worth toward self, others, or toward the world. REBT posits that a person cannot be rated dichotomously as good or bad since human beings are too complex to be evaluated in such a manner; instead, evaluation could only occur regarding specific behaviors of an individual in a specific situation.(Buschmann et al.,2017)

6.5 Psychotic Depression & melancholia/somatic Syndrome

In the early 20th century, psychiatrists debated whether depression was a single disorder or whether there were distinct disorders such as psychotic/endogenous depression and neurotic/reactive depression. According to Paykel(2008) ,this controversy was prominent in British psychiatry during the 1920s and 1930s, diminished during World War II, and resurfaced through empirical studies in the 1960s.

The terminology surrounding depression was unclear, with "psychotic" referring to severe disorders with delusions and hallucinations, and "neurotic" to milder disorders without these symptoms, often related to a vulnerable personality. "Endogenous" and "reactive" described the absence or presence of stress in daily life. Over time, these terms partially merged, giving rise to a three-part concept: (i) the absence of stress in daily life, (ii) a severe clinical picture with symptoms such as delusions, morning worsening, and somatic complaints, known as endogenous or endogenous depression, and (iii) a stress-prone personality type, associated with reactive or neurotic depression.

Over time, the concept of psychotic depression has been distinguished from endogenous depression. Psychotic depression is now recognized as a distinct form of major depression, characterized by delusions or hallucinations, particularly if they correspond to the person's mood. This distinction is supported by evidence, such as the fact that treatment of psychotic depression with electroconvulsive therapy (ECT) or antipsychotic medications is more effective than treatment with antidepressants alone.

The classification of endogenous depression and its opposite remains challenging due to unclear terminology and overlapping features. While studies from the 1960s and 1970s often identified a dimension resembling psychotic or melancholic depression, neurotic depression did not emerge as a distinct group, suggesting its heterogeneity. Endogenous depression is linked to specific neuroendocrine abnormalities and may show a better response to antidepressants, although this is not definitive. The boundaries be-

tween these depression types are blurred, with common overlaps, particularly between psychotic depression and melancholia, making clear distinctions difficult

The terminology for depression remains problematic. The term "neurotic" has fallen out of use, particularly in American psychiatry, due to its varied meanings and associations with psychoanalysis. Disorders like dysthymia and cyclothymic personality are now classified as mood disorders, such as dysthymic and cyclothymic disorder. The term "endogenous" has been discarded in favor of symptom-based descriptions. "Melancholia" is preferred over "somatic depression" in English due to its clearer usage, although its historical meaning of "black bile" is now forgotten. The future of these classifications in upcoming revisions is uncertain, but "melancholia" remains widely used in research and literature, with strong support for its retention.

Conclusion

Depression is a multifaceted mental health condition influenced by biological, psychological, and social factors. It impacts individuals regardless of gender, age, or background, and can manifest as chronic or recurrent episodes, significantly hindering a person's ability to manage daily tasks. The variety of clinical presentations, which can include atypical or misleading symptoms that vary with age, can complicate the diagnostic process. Depressive disorders rank as the third most disabling illness and represent a significant public health challenge.

Unit 6: Geriatric Psychopathology

Physical and Psychological Problems of the Elderly

Objectives

By the end of these lectures, students will be able to:

- Gain a deeper understanding of the physical and psychological problems of older people.
- Provide a general description of dementia and Alzheimer's disease.
- Identify and address health disparities associated with Alzheimer's disease and other dementias.

Introduction

Geriatric psychopathology is a field that focuses on the mental health challenges faced by older adults, including physical, psychological, and neurological issues like dementia, Alzheimer's disease, depression, anxiety, and loneliness. It highlights the similarities and differences in psychopathology across age groups, emphasizing the need for healthcare professionals to provide effective treatment and support for the elderly.

The ageing of the world's population is a global phenomenon with extensive economic and social consequences. The ratio of the elderly population (60 years and older) is now 1 in 10. By the year 2050, the ratio would have increased up to 1 in 5. This older population will continue to age and currently, people aged 80 years and older represent 11% of the population aged 60 and above. By 2050, those over 80 will represent 27% of this older population.(Maideen et al.,2014,p.52)

Old age is the end stage of human life as well as it is not a disease. The main characteristics of old age that, it is a period of decline, poor adjustment, health problems, and

changes in the body cells as a result of aging process and depression. The process of aging is related to biological, mental, and social changes which cause susceptible conditions to get physical, social, and psychological health problems. It was estimated that 80% of the elderly live with chronic diseases such as arthritis, hypertension, diabetes, heart disease, and vision and hearing disorders.

Furthermore, elderly people face a lot of problems such as psychological health problems as anxiety and depression, which are more popular among old age . The most common mental health disorder is severe cognitive impairment or dementia among the elderly, which is caused by Alzheimer's disease. Furthermore depression and mood disorders are widespread among elderly. Also anxiety is one of the more prevalent mental health troubles among the older adult.(El-Zeftawy & Mohamed,2018,pp. 236–237)
The lectures aim to discuss complex health issues of older people, including common psychological and mental health disorders such as dementia and Alzheimer's disease.

1 Defining old age

Giving universal definition of old age becomes challenging as most countries have adopted an arbitrary chronological age of 60 or 65 as criteria to describe the elderly population of their countries . It can be used as the threshold criterion because most people are likely to retire from their services or jobs at this age. The developed nations have opted for the chronological age of 65 years to define elderly or older adults, whereas most other countries have taken 60 years . However, there are universally accepted definitions for old age, but it is still inconclusive and debatable at what age a person becomes old. The common use of a calendar age can give a threshold, but it may or may not be uniform with the person's biological age.(Sharma and Morishetty,2022,p.2)

2 Etiology

2.1 Biological Theories Of Aging

This theory tries to explain why physical changes occur in old age. Researchers are trying to determine the most effective biological factor affecting longevity. It has been found that all members of a species suffer from a gradual and progressive decline in function over time due to the structure of their habitat. Many biological views of aging overlap, as they often accept that aging-causing changes occur at the cellular level. Some theories of aging look at aging from a genetic perspective.

2.1.1 Programmed theory

Suggests that each person have a biological clock that starts working at fertilization. According to this theory, each individual has a genetic program that programs the number of cell divisions that are unknown but predetermined. As the (genetic) program indicates, a person experiences predictable changes such as thymus shrinkage, menopause, skin changes, and gray hair. An almost similar theory is program termination theory, which suggests that each individual has a limited amount of genetic material that, activated over time, leads to certain changes seen in old age, and limits a person's life.
Molecular Theories: It is suggested that aging be controlled by genetically engineered genetic material

- **Error Theory:** It suggests that errors in RNA protein synthesis lead to errors in the body's cells that lead to progressive deterioration of biological function.
- **Somatic Mutation Theory:** It is similar to the previous theory, but suggests that aging occurs due to DNA damage caused by exposure to radiation or chemicals. This damage causes abnormalities in the chromosomes that lead to disease or subsequent dysfunction in life.

- **Cellular theories:** It is suggested that aging is a process that occurs due to cell damage. When a certain number of cells are damaged, all bodily functions are reduced.

- **Free Radicals Theory:** Explains cell damage. Free radicals are unstable molecules that are produced by the body during natural processes of respiration and metabolism, or by exposure to radiation and pollution. Free radicals are thought to damage cells, DNA and the immune system. The high accumulation of free radicals in the body seems to be involved in or cause the physiological changes of old age and various diseases such as arthritis, circulatory diseases, diabetes and atherosclerosis. The free radical lipofecin causes the formation of oily pigmented granules that cause age spots in the elderly .People who support this theory, It is suggested that the number of free radicals can be reduced by using antioxidants such as vitamins, carotenoids, selenium and plant foods.

- **Crosslink theory:** Or connective tissue theory, which suggests that DNA and connective tissue cell molecules interfere with free radicals to form bonds that reduce the tissue's ability to repair itself. This leads to age-related skin changes such as dryness, wrinkles and reduced skin elasticity.

- **Clinker Theory:** It is a theory that combines theories of body evolution, free radicals, and crosslinking, stating that chemicals created by metabolism accumulate in normal cells and damage organs such as muscles, hearts, nerves, and the brain.

- **Wear-and-tear theory:** The human body assumes a machine that loses its function when its parts wear out. As people age, cells, tissues, and organs are damaged by internal and external stresses.When different parts of the body are severely damaged, the overall function of the body decreases. This theory also suggests that health care practices reduce the rate of burnout and destruction and lead to better and longer functioning of the body.

- **Immunologic theory:** Suggests that aging is a function of immune system changes. According to this theory, the immune system - an important defense mechanism of the body - is weakened over time and the elderly become more prone to disease. Immunity theory also suggests that an increase in autoimmune diseases and allergies in old age is caused by changes in the immune system.(karamivand & Mohamadi,2022,p.11)

2.2 Psychosocial Theories Of Aging

2.2.1 Classical Theories

Theory of Disengagement: Was developed by Cummings and Henry . From this theoretical perspective, older adults willingly give up roles and disengage from society as they age . Disengagement Theory has been used to explore role changes in late life such as widowhood . However, it is not prevalent in recent gerontological research, and theorists argue that it is not in fact a component of successful aging . Critics of the theory argue that disengagement is not universal among all older adults and that when the theory is tested with older adults, there is little evidence to support disengagement .
Activity theory: The Activity Theory was first introduced by Cavan et al. and Havinghurst and Albrecht . General principles guiding the theory assert that older adults naturally gravitate toward and participate in community, society, and social roles . An increased activity level is associated with greater life satisfaction and consequently greater well-being in older adulthood . However, critiques of the theory include concern that there are other factors that may explain the relationship between life satisfaction and increased activity level (e.g. socioeconomic status, personality, lifestyle, etc. The Activity Theory has been used extensively in research and is often used when assessing or predicting successful aging. Researchers have noted significant evidence of Activity Theory as it relates to well-being and survival in older adults.

2.2.2 Modern Theories

Modernization Theory was developed by Cowgill and Holmes and states that as society becomes more modern, the status of older adults declines . For example, the usefulness of older adults eroded with the shift from an agricultural to a more industrial society . The theory has been used to understand negative attitudes toward aging, as well as family relationships and family caregiving dynamics. Achenbaum and Sterns note there needs to be more agreement regarding when modernization first began as well as classifying stages within modernization. The authors go on to discuss the complexities of how modernization has affected various age groups in different ways. Consequently, the main criticisms of the theory are that it is broad and needs to be more appropriately specified.

Continuity Theory, first developed by Atchley . Diggs asserts that even as older adults age they continue to be interested in and participate in previous hobbies, goals, roles, and activities. Continuity can be looked at from both internal and external viewpoints. Internally, older adults may be persuaded to continue to engage in previous activities due to the sense of stability and security they provide . External continuity may have more to do with fulfilling expectations related to previous roles or behaviors . Critics of this theory maintain that Continuity Theory may be more applicable and useful for healthy older adults. For example, Diggs noted the difficulties of maintaining continuity when faced with medical conditions, disabilities, or memory impairment. Continuity Theory has often been paired with Activity Theory in gerontological research. Similar to Activity Theory, Continuity has also been included in literature on successful aging as well as lifelong learning.

Socio-emotional Selectivity Theory was proposed by Carstensen et al. and states that when individuals are faced with limited time, they prioritize emotionally meaningful experiences and relationships rather than focusing on more future-oriented goals.. Carstensen et al. goes on to explain that changes in priorities are also likely to influ-

ence social networks (i.e., paring down a social network to include only the closest of relationships is thought to facilitate the emotion regulation that may be present when faced with impending mortality). Socioemotional Selectivity Theory has been used to explore the social networks and relationships of older adults , as well as motivation and emotion .One criticism of the theory is that, although many of the findings have been validated in research (i.e., older adults narrowing their social networks), many of the studies only assess this from a cross-sectional perspective. It is possible that there are cohort differences in preferences for social networks and goal-setting behaviors.

2.2.3 New Period Theories

Selective Optimization with Compensation: Baltes and Baltes developed the Selective Optimization with Compensation Theory and proposed older adults can successfully adapt and cope with growing older by focusing on the gains and strengths (rather than losses) and engage in compensation strategies when encountering challenges. This theory has been used as a framework to help understand successful aging in older adults in a number of different ways, including adapting to disability and memory decline . A criticism of the theory is that it is a bit reactive rather than proactive. Ouwehand et al. argue that theories or models that focus on proactive coping may lead to greater understanding of successful aging.

Theory of Gerotranscendence: Lars Tornstam first developed the Theory of Gerotranscendence in 1989. The theory includes three specific levels including the (1) cosmic; (2) the self; and (3) social and individual relations . The cosmic level is related to perceived changes to time, space, and decreased fear of death. Individuals take on new characterizations of the self, including increased understanding of hidden aspects of the self. There is also a significant shift away from the self and on to others (i.e., altruism). Social and individual relations may refer to increased focus on solitude and pondering as well as some role relinquishment. The theory has been used to better understand

the importance of reminiscence in older adulthood , spirituality and life satisfaction . Some researchers have been critical of the view that spirituality may change with age. Instead, Dalby pointed out that dimensions of spirituality may change due to other reasons. Likewise, questions surrounding the universality of the theory have been raised. For example, Jewell theorized that gerotranscendence may be dependent on the individual or culture.(Heinz et al.,2017,p.p 3-5)

3 Negative effects of aging on health

At the biological level, aging results from the accumulation of molecular and cellular damage over time. This results in a gradual decline in physical and mental capacities and an increase in the risk of disease. In addition to biological changes, retirement, loss of purpose in life, relocation to more suitable housing, and the death of a friend or partner also often result in psychological damage. In addition to physical and mental decline, social restrictions also result in a diminished quality of life.

3.1 Cellular Changes

First, with aging, the oxygen supply to all organs and tissues and the partial pressure of oxygen in tissues decrease, resulting in hypoxia. It is then thought to be involved in the development of inflammatory diseases, tumors, and cardiac disease . Excessive production of reactive oxygen species also leads to the destruction of nucleic acids and proteins, thereby altering cellular structures and functional outcomes. The detrimental effect on the organism caused by such oxidative reactions is called oxidative stress. It causes aging and chronic degenerative diseases such as cardiovascular disease, diabetes mellitus, and chronic kidney disease, Alzheimer's disease (AD), Parkinson's disease, and other neurodegenerative diseases.

Advanced glycation end-products (AGEs) is a general term for heterogeneous deriva-

tives produced by non-enzymatic reactions of reducing sugars with proteins. It has recently been suggested that AGEs are involved in the pathogenesis of chronic hyperglycemia and age-related diseases. The accumulation of AGEs and their derivatives can modify proteins and could promote aging by activating several inflammatory signaling pathways via AGEs-specific receptors.

3.2 Chromosome Changes

Telomeres are structures at the ends of chromosomes that shorten with each cell division. Shortening of telomeres, which are specialized nucleoprotein structures at the ends of linear chromosomes, has been linked to aging . When telomeres do not function, chromosomes lose their protective structure, and fusion and breakage phenomena occur, leading to further genomic instability such as cell arrest and death . Additionally, impairment of the telomere function, coupled with impairment of the senescence/apoptosis response, causes chromosomal instability.

3.3 Psychological Changes

In addition to the above-mentioned physiological changes, various age-related events negatively impact mental health. Loss of a role or purpose in life after retirement, the independence of children, or the death of a partner or good friend can cause psychological harm . Except for those who can retire with sufficient savings, many older adults could experience financial hardship due to a decrease in income . It is easily perceived that these factors can negatively impact health.(Noto,2023,pp. 2-3)

4 Diseases likely to occur with age

According to World Health Organization(2004), Normal ageing is not a disease but eventually leads to structural and functional decline and involves increased suscepti-

bility to diseases. Ageing seems not to affect all physiological functions to the same degree, so that the total ageing rate of different organisms will differ. Factors related to ageing changes can be determined as intrinsic and extrinsic. The intrinsic factors are related to normal ageing such as genetic, while extrinsic factors include the environment and the lifestyle. The physiological changes occur in all body systems such as musculoskeletal, cardiovascular, respiratory, neurological and gastrointestinal systems. Significantly, these changes lead to diseases. For example, cardiovascular changes during old age, such as thickening of the blood vessels and of the ventricular free wall and the septum, lead to stiffness and decrease in contractility of the heart, and are considered as factors resulting in coronary artery disease and hypertension.

Ageing produces changes in the respiratory organ itself and in related organs, thereby resulting in the decline of lung function, which is a significant factor of chronic obstructive pulmonary disease, emphysema, asthma, and chronic bronchitis among the elderly. Agerelated neurological problems include dementia and delirium due to the loss of neurons.

Disorders of the gastrointestinal system related to normal ageing changes include peptic ulcers, loss of appetite, dysphagia, hernia, carcinoma, and gastritis. The major change in the gastrointestinal system is the decrease of hydrochloric acid and atrophy of the gastric mucosa. Renal failure, prostatic hypertrophy, urinary incontinence, and vaginitis are common problems of the genitourinary system among the elderly. There are many age-related changes in the genitourinary system, such as loss of nephrons, loss of renal mass, the thickening of the glomerular and tubular basement membrane. A normal ageing change in the endocrine system is hormonal secretion, and the sensitivity of hormonal stimulation of the target organs decreases. This change leads to the disease of diabetes mellitus and thyroid diseases.

Not only physiological changes, but also psychological changes occur in older people. These changes are considered to be factors associated with illnesses among the

elderly. Depression and anxiety are the most common psychological disorders.

5 Age-related psychological disorders

Manifestations of mental disorders may be different in the elderly, compared with younger age groups, and there may be difficulties in separating symptoms of mental disorders from those occurring in normal aging. For example, there is an overlap in symptoms of depression and those occurring in physical disorders and in normal aging (for example, loss of appetite, tiredness, and sleep disturbances). This may lead not only to overdiagnosis but also to underdiagnosis if depressive symptoms are thought to be due to physical disorders or normal aging.

Depression may also have different manifestations in the elderly. For example, elderly people may present with a smaller number of symptoms66 or one dominating symptom. Depressed elderly people may also more often show aggressiveness, cognitive difficulties, and loss of interest and apathy, and less often symptoms of depressed mood. However, it has to be emphasized that the symptoms of depression most often are similar in the old and in the young. Depression is reported to have a poor rate of recovery in the elderly, although it is unclear whether the recovery rate is worse than for younger depressed people, and about one-third of depressed elderly people still have depression at 1 to 3 years of follow-up. In contrast, social phobia seems to have a good prognosis in the elderly, with 50% being free of social fear at 5-year follow-up.

Also anxiety disorders may have different manifestations among the elderly, with fewer symptoms, less somatic and autonomic symptoms, and less avoidance, and more agitation, irritability, talkativity, and tension, and with more somatization. However, most anxiety disorders have similar symptoms in the old and in the young.

Compared with early onset psychosis, people with late-onset psychosis have better preserved personality, less affective blunting, less formal thought disorder, more in-

sight, and less excess of focal structural brain abnormalities and cognitive dysfunction, compared with age-matched control subjects. Also late-life psychosis may show less symptoms, and one symptom may dominate the picture.

Finally, criteria for mental disorders are often validated in younger age groups, and their use in the elderly has therefore been questioned.(Skoog,2011,pp.389- 390)

6 Structural brain disorders

Structural brain changes become more common with increasing age,and have been associated with mental disorders in old age by several investigators. Late-life depression, especially major depression, has been associated with ventricular enlargement, changes in the caudate nuclei, and the putamen, and with atrophy in the frontal, temporal, and parietal lobes. However, most studies on the association between brain atrophy and depression in the elderly have been cross-sectional and performed in clinical samples. One longitudinal population based study reported an association between temporal lobe atrophy on CT at baseline and development of major depression during a 5-year follow-up. Another longitudinal population-based study reported a cross-sectional association between temporal and parietal lobe atrophy assessed with MRI at baseline and concurrent depressive symptoms, but no association with depression occurring during follow-up. A third longitudinal study in elderly without dementia examined the association between mean depressive symptom scores over time and change in brain atrophy on MRI during 9 years. Cross-sectional associations between temporal and frontal lobe atrophy and depressive symptoms, and a longitudinal association between volume decline in frontal white matter and depressive symptom score over time were reported.

The cellular mechanisms that underlie the association between brain atrophy and depression in the elderly remain largely unknown. Postmortem studies have reported on cellular alterations such as neuronal death, neuronal shrinkage, decrease in dendritic

and glial density, and cell death in the frontal cortex and hippocampus in the elderly with major depression.

Anxiety disorders have been related to brain changes in younger age groups. In relation to anxiety disorders in the elderly, worries in GAD were associated to decreased volume in the prefrontal cortex.

Subtle brain changes, such as degenerative or vascular changes, have also been hypothesized to enhance vulnerability to psychotic symptoms in the elderly, but reports are disparate. Some studies report a higher ventricle to-brain ratio, larger third ventricle volume, and volume reductions of the left temporal lobe or superior temporal gyrus. In a study on people aged 85 years, basal ganglia calcifications, but no other brain changes, were associated with increased frequency of psychotic symptoms.(Skoog, 2011, p.391)

Neurological disorders: Dementia disease

1 Definition

Dementia refers to a clinical syndrome characterized by progressive cognitive decline that interferes with the ability to function independently. Symptoms of dementia are gradual, persistent and progressive. Individuals suffering from dementia experience changes in cognition, function and behaviour. The clinical presentation of dementia varies greatly among individuals, and the cognitive deficits it causes can present as memory loss, communication and language impairments, agnosia (inability to recognize objects), apraxia (inability to perform previously learned tasks) and impaired executive function (reasoning, judgement and planning). Cognitive impairment stems from injury to the cerebral cortex caused by synaptic failure, inflammation and change in cerebral metabolism.(Duong et al.,2017,p.118)

Dementia is generally defined,in the DSM5,as the “loss of intellectual abilities (medically called cognitive function) of sufficient severity to interfere with social or occupational functioning”.

2 History Of Nosological Classification

According to The Swedish Council on Technology Assessment in Health Care (2008), dementia has often been classified based on neuropathological criteria and presumed etiological factors rather than clinical characteristics. Apoplexy was a well-known clinical phenomenon even in antiquity, as were its sequelae, including paresis and changes of mentation and behavior. Thomas Willis offered a description of vascular dementia (VaD) in 1672 and made crucial observations on cerebrovascular circulation.Hemorrhage long remained the dominant pathophysiological explanation of stroke. The early 19th

century saw the introduction of the concept of softening, as well as its association with arterial occlusion and infarction in stroke . In an 1854 classification of mental diseases , Baillager distinguished paralysie générale from démence incoherente and démence simple. Kahlbaum described vesania progressiva apoplectica, as well as dementia paralytica, dementia aquisita and presbyophrenia . The 1896 edition of Kraepelin's psychiatry textbook broke organic brain syndromes down into diffuse and localized brain diseases, strongly associating dementia with aging . The work of Alzheimer and others modified this perspective, and the 1910 edition of the textbook presented AD as a presenile dementia, a term coined by Binswanger in 1894 . However, cerebral arteriosclerosis was regarded as the major cause of organic dementia, while post-apoplectic and arteriosclerotic dementia were used synonymously.

The classification of dementia has been a controversial issue since the evolution of modern neuropsychiatry in the late 19th century. Arnold Pick reported an association between circumscribed cortical degeneration, aphasia and behavioral changes in some cases of dementia . Alzheimer presented a pathological account of this lobar atrophy in 1911. Onari and Spatz and Stertz established the clinicopathological entity of Pick's disease in the 1920s. Schneider suggested a threestage model, dominated by frontal lobe symptoms, to describe its clinical course . The concept of frontotemporal dementia (FTD) and its diagnostic criteria have evolved mainly during the last two decades based on several clinical and pathological studies . Clinical and pathological consensus documents have described the spectrum of FTD, and frontotemporal lobar degeneration (FTLD) later on, more recently including classification attempts based on biomarkers such as genetics.

The 5th edition of offers guidelines for diagnosis of one type of primary degenerative dementia – dementia of Alzheimer type (DAT) and one type of VaD – multiinfarct dementia (MID) . These two dementia disorders are subclassified as "uncomplicated" or "combined with delirium, delusions or depression". Such subclassification that empha-

sizes the natural course and variability of a progressive disease had already been called into question by Alzheimer . ICD-10 offers four main categories of dementia: DAT, VaD, dementia in diseases specified elsewhere (such as Pick's disease and Creutzfeldt-Jacob's disease), and dementia "not otherwise specified" . DAT is subclassified with respect to early vs late onset, typical vs atypical clinical features, and pure or combined with VaD. VaD is broken down in terms of type of onset and predominant involvement (cortical vs subcortical). A 1990 Swedish consensus report from dementia research centers in Lund, Göteborg, Stockholm and Umeå offered a clinical classification based on predominant clinical features, as well as type and location of the brain disease . Diagnosis should rely on a thorough analysis of the patient's history and a standardized clinical examination. Three main etiology-based categories were primary degenerative dementia, VaD and other secondary dementias. Primary degenerative dementia was broken down into 1) frontotemporal, 2) temporoparietal, 3) subcortical and 4) other predominance. The 1994 LundManchester consensus statement on FTD and the 1998 consensus on FTLD further elaborated the criteria for the first group.

3 Symptoms of Dementia

The International Psychogeriatric Association has for many years recognized the importance of behavioral and psychiatric problems of dementia patients. It is based on the understanding that manifestation of signs and symptoms of dementia patients is very different between subjects. In order to elucidate these versatile signs and symptoms, biological, psychological, social, and ethical factors should be integrated into the research. Signs and symptoms of dementia may be caused by neuronal degeneration in the brain, but manifestation of these signs and symptoms is not the simple reflection of neuronal degeneration but the mode of manifestation should be regulated by psychological and social factors. 'Behavioral and psychiatric problems of dementia' is now substituted

by the new term 'behavioral and psychological symptoms of dementia' (BPSD), which was originally proposed in a paper by Consensus group of International Psychogeriatric Association. Behavioral and psychological symptoms of dementia is defined as symptoms of disturbed perception, thought content, mood or behavior that frequently occur in patients with dementia. Behavioral and psychological symptoms of dementia can be grouped into behavioral symptoms usually identified on the basis of observation of the patients, including physical aggression, screaming, restlessness, agitation, wandering, culturally inappropriate behaviors, sexual disinhibition, hoarding, cursing, and shadowing. The other groups of symptoms are psychological, usually and mainly assessed on the basis of interviews with patients and relatives, including anxiety, depressive mood, hallucinations and delusions.(Shinosaki et al.,2000, p.613)

4 Dementia Subtypes

There are over 400 subtypes of dementia, with the most common form being Alzheimer's disease, followed by vascular dementia and mixed Alzheimer and vascular dementia. Other common forms of dementia include Dementia with Lewy Bodies (DLB), Fronto temporal Dementias and less common types such as Huntington's disease, Parkinson's disease dementia and Creutzfeldt-Jakob disease (O'Shea et al.,2018)

Table 6.3. Common subtypes of dementia

Dementia type	Common symptoms and signs
Alzheimer's disease	Gradual onset with continuing decline (over 2–20 years). Short-term memory loss is a classic early feature followed over time by problems with attention, orientation, language, comprehension, visuo-spatial Gradual onset with continuing decline (over 2–20 years). Short-term memory loss is a classic early feature followed over time by problems with attention, orientation, language, comprehension, visuo-spatial perception as well as mood changes.
Vascular Dementia	Vascular Dementia exhibits a more stepwise decline. The person may experience gait abnormalities, display signs of vascular disease and focal neurological signs
Mixed Dementia	In the most common form of mixed dementia, the abnormal protein deposits associated with Alzheimer's disease coexist with blood vessel problems linked to vascular dementia. Alzheimer's disease can also coexist with Lewy bodies.
Dementia with Lewy Bodies	Person may have fluctuating cognition / alertness, hallucinations that are typically visual (but can be auditory, tactile, etc.) and / or evidence of Parkinsonism.
Parkinson's Disease Dementia	Unlike Dementia with Lewy Bodies, movement problems usually precede cognitive symptoms by years. Orientation is typically well preserved and memory issues reflect retrieval more than memory storage issues.

Dementia type	Common symptoms and signs
Progressive Supranuclear Palsy	Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD) are often classified as Parkinsonian disorders, but are due to tau pathology.
Corticobasal Degeneration	Features overlap with a frontal-type dementia, often with impulsivity, speech fluency issues, swallowing difficulties and prominent falls along with the hallmark vertical gaze palsy in PSP and apraxia in CBD).
Frontotemporal Dementia (FTD)	Generally develops at a younger age (around 60), is more likely to be hereditary and is the cause of 10-12% of cases of dementia with onset under 65 years. Can present with changes in behaviour such as disinhibition, loss of social awareness and loss of insight, and / or with speech being prominently affected (problems generating words / sentences or in understanding words / sentences). Can overlap with Motor Neurone Disease in up to 15% of cases.
Huntington's disease (HD) dementia	Along with the hallmark involuntary motor movements (chorea), people with HD can develop depression, obsessive-compulsive thoughts and personality changes. In HD dementia, executive function is particularly impaired, along with language and memory.
Alcohol related cognitive syndromes	A spectrum of disorders ranging from A spectrum of disorders ranging from cognitive impairment which can stabilise or improve with abstinence, through to Wernicke-Korsakoff Syndrome, which is specifically a consequence of thiamine deficiency and frequently results in irreversible dementia characterised by profound anterograde amnesia and confabulation.

(Begley et al.,2023, p.20)

Dementia of the Alzheimer's type, typically referred to as Alzheimer's disease (AD), and the vascular dementias (VaD), including multinfarct dementia, represent the most common irreversible dementia syndromes . Less common dementias include dementia

due to Parkinson's disease, Lewy body disease, Pick's disease, frontal-temporal dementia and progressive dementing disorders such as Huntington's disease and Creutzfeldt-Jakob disease. All dementias are characterized by impairment in multiple cognitive domains including memory, language, problem solving, judgment and abstraction, visuospatial abilities, and skilled movement . Dementias also may be associated with psychiatric symptoms (e.g. hallucination, delusions), behavioral disturbances, (e.g. agitation), personality changes (e.g., irritability), and disturbances of affect (e.g. depression, emotional liability). These changes can be viewed as both a manifestation of the underlying disease process and a psychological reaction to it.

The main distinction between AD and VaD is disease course, with AD showing a pattern of steady progressive deterioration whereas VaD may show a more stepwise deterioration. When differences in psychiatric symptomatology and behavioral problems are found between diagnostic groups, the differences are more often attributable to differences in severity of impairment or stage of the disease, rather than to diagnosis.(Kasl-Godley & Gatz,2000,p.756)

5 Theoretical Approaches

Research indicates that dementia symptoms may be the result of biological dysfunctions in the brain. Emphasis will be placed on psychopathological approaches to understand the fundamental mechanisms of dementia, as pathophysiological and neurobiological factors differ among different types of dementia.

5.1 Psychodynamic Conceptualization Of Dementia

There have been a number of efforts to describe dementia in terms of psychodynamic, ego analytic, and ego developmental concepts. Dementia results in weakened ego functioning, diminished mastery over the environment and increased dependency. These

changes may trigger unresolved psychodynamic conflicts depending on the adequacy of defenses . In early stage dementia, the weakened ego tries to protect itself from current and subsequent losses, often through defense mechanisms such as denial, projection, splitting, or withdrawal. As the dementia progresses, the individual struggles to maintain a sense of self and becomes increasingly dependent. The person may show an increasing need for reassurance and shadowing of others. Eventually defense mechanisms fail and the individual becomes more distressed, showing aggression, agitation, hostility, outbursts, catastrophic reactions, isolation, despair and loneliness.

Self psychologists and object relations theorists emphasize the ways that dementia compromises one's capacity to maintain a sense of self through internalized selfobject relations. The individual must rely increasingly on others to provide the ego functions that maintain a sense of self . The result of this increased reliance on others is insecurity, fear of separation, and the need for constant contact. The merging of past experiences with the present, stemming from memory decline, can support self-concept and self-worth if the images of the past evoke a sense of pleasure and accomplishment; it also may fragment the self, (e.g., if dead or absent individuals are thought to exist in the present or, if people from the past are not recognized or remembered in the present). As the dementia becomes more severe, even the ability to use others as a means to enhance one's sense of self becomes impaired, resulting in extreme confusion, anxiety and psychotic defenses.(J. Kasl-Godley & Gatz,2000,p.758)

5.2 Behavioral Conceptualization Of Dementia

The main behavioral theories or models that have been proposed are :

5.2.1 The Unmet Needs Model

The model postulates that the dementia process results in a decreased ability to meet one's needs because of an increasing difficulty in communicating these needs, and a

decreased ability to provide for oneself . The needs may pertain to pain/ health/ physical discomfort, mental discomfort, the need for social contacts, uncomfortable environmental conditions, or an inadequate level of stimulation. According to the Unmet Needs Model, problem behaviors result from an imbalance in the interaction between lifelong habits and personality, current physical and mental states, and less than optimal environmental conditions. When a person has needs that cannot be expressed verbally, they often communicate through their actions. Babies are unable to communicate their needs so they use actions such as: crying, tantrums, throwing things, etc. Individuals with dementia face similar situations because the illness affects their ability to organize their thoughts or find words quickly. Unable to express their needs to their caregiver, they may use other strategies like yelling, agitation, aggression, etc.

5.2.2 Progressive Lower Threshold

The model holds the assumption that people with Alzheimer's disease and related dementia ADRD have difficulty in comprehending, receiving, processing, and responding to the stimuli from the environment . People with dementia face such difficulty because of the continuous deterioration in cognitive, affective, and functional abilities. The severity and frequency of behavior vary according to environmental factors and the stage of dementia in which the person is. As the stages of dementia advance correspondingly, the behavior becomes more and more typical. Person with dementia encounters stress on a daily basis and these stress inducers can be internal as well as external. These stress inducers are thought to be at the root of behavioral disturbances such as hitting, resisting care, yelling, anxiousness, pacing, and sun downing. Everyone has a point when they become agitated at something within the environment or something internal. Some have a higher threshold for stress than others. For people with dementia, the threshold for agitation is very low. When dealing with stress in their environment the person with dementia can become overwhelmed and act out as a result.(Javed & Kakul,2023,p.111)

6 Stages Of Dementia

Still the progression stage of dementia has been discussed with the Health professionals -which refers to how far a person's dementia has developed. If the disease stages would be considerable that could help to the health professionals and caregivers to determine the appropriate treatment approach. Frequently the disease stages referred to as "early stage", "middle stage" or "late-stage" dementia, but often a more exact stage is assigned, based on a person's symptoms. Commonly used scales is the Global Deterioration Scale for Assessment of Primary Degenerative Dementia- it divides the disease process into seven stages based on the amount of cognitive decline. The GDS is most relevant for people who have Alzheimer's disease, since some other types of dementia (i.e. Frontotemporal dementia) do not always include memory loss.

The global deterioration scale for assessment of primary degenerative dementia (GDS) is also known as the Reisberg Scale. That can distinguish stages of dementia and on the basis of patients' characteristics (Pathak KP, 2018, p14).The phases of advancing dementia are comprehensively outlined in the table below.

Table 6.4. Stages of dementia

Stages	Signs and symptoms
Stage 1	In the first stage the person shows normal function, has no memory loss, and is mentally healthy. People with no dementia would be considered to be in Stage 1, is called no cognitive decline(no dementia).
Stage 2	In the second stage is used to describe normal forgetfulness associated with aging; for example, forgetfulness of names and familiar objects. Symptoms are not evident to loved ones or the physician. That is called very mild cognitive decline(no dementia).
Stage 3	The 3rd stage of dementia includes increased forgetfulness, slight difficulty concentrating, decreased work capacity and its average duration remains up to 7 years. People may get lost more often or have difficulty finding the right words. At this stage, a person's loved ones will begin to notice a cognitive decline. It is called mild cognitive decline (no dementia).

Stages	Signs and symptoms
Stage 4	This stage includes difficulty concentrating, decreased memory of recent events, and difficulties managing finances or traveling alone to new locations. The average duration is 2 years. People have trouble completing complex tasks efficiently or accurately and may be in denial about their symptoms. They may also start withdrawing from family or friends because socialization becomes difficult. At this stage, a physician can detect clear cognitive problems during a patient interview and exam. It is called moderate cognitive decline(no dementia).
Stage 5	This stage duration holds at least 1.5 years. People in this stage have major memory deficiencies and need some assistance to complete their daily activities (dressing, bathing, preparing meals). Memory loss is more prominent and may include major relevant aspects of current lives; for example, people may not remember their address or phone number and may not know the time or day or where they are. It is called moderately severe cognitive decline (no dementia).
Stage 6	People in Stage 6 require extensive assistance to carry out daily activities. They start to forget names of close family members and have little memory of recent events. Many people can remember only some details of earlier life. They also have difficulty counting down from 10 and finishing tasks. Incontinence (loss of bladder or bowel control) is a problem in this stage. Ability to speak declines. Personality changes, such as delusions (believing something to be true that is not), compulsions (repeating a simple behavior, such as cleaning), or anxiety and agitation may occur. Average duration: 2.5 years. It is called severe cognitive decline (middle dementia) (mild-stage).
Stage 7	People in this stage have essentially no ability to speak or communicate. Its average duration is 2.5 years. They require assistance with most activities (e.g., using the toilet, eating). They often lose psychomotor skills, for example, the ability to walk. It is called very severe cognitive decline (late-stage dementia).

(Pathak,2018,p.14)

7 Differential Diagnosis

The leading aetiology of dementia, accounting for at least half and possibly two-thirds of cases, is Alzheimer's disease(AD). Primary dementia with no other reasonable explanation is usually presumed to be AD. In AD, the anterograde amnesia may be moderate to severe before there is obvious impairment of other cognitive domains. The dementia of Alzheimer type, amnesic primary dementia, is the modal form of dementia, and departures from this profile (i.e. 'disproportionate' impairments in some other domain of cognition) raise the possibility of another diagnosis. In terms of prevalence, the second tier of dementing disorders is occupied by vascular dementia, Frontotemporal lobar degeneration FTLD, and dementia with Lewy bodies DLB, all of which have been claimed to be the secondmost common cause of dementia.

Vascular dementia is usually suggested by a history of stroke or significant cardiovascular disease, and compatible findings on imaging studies. FTLD may be suggested by a dysexecutive profile, but is probably most commonly recognized on the basis of the characteristic lobar atrophy onimaging studies. dementia with Lewy bodies DLB is suggested by prominent psychiatric symptoms and parkinsonism, but may be difficult to distinguish from AD and idiopathic Parkinson's disease IPD. All other causes of dementia are quite uncommon. Among the uncommon causes, hydrocephalic dementia (associated with gait difficulty and urinary incontinence), Corticobasal degeneration CBD (with asymmetric dopa-unresponsive parkinsonism, and apraxia), and Creutzfeldt– Jacob disease CJD (associated with subacute course and often myoclonus) have the most distinctive presentations. Reversible secondary dementiais quiteuncommon,probably accounting for about 1–2% of all cases of dementia.(Grabowski & Damasio,2004,p.7)

Neurological disorders: Alzheimer Disease (AD)

1 Definition

AD is the most common cause of dementia, a neurodegenerative condition that is insidious and progressive. Impaired new learning and recall (amnestic loss not improved with prompting) displayed as a pervasive forgetfulness is an early feature. Communication changes are noted, with shrinking vocabulary and expressive or word-finding difficulties. Visuoconstructional deficits, spatial disorientation and dyspraxia become evident, particularly with less ability to judge distance with tasks, such as driving, and the person can become lost within familiar environments. The management of a person with AD is often hindered by variable lack of insight or anosognosia.(LoGiudice & Watson,2014,p.1067)

2 Brief History

According to the World Health Organization (2017), the second edition of the Diagnostic and Statistical Manual of the American Psychiatric Association in 1968 introduced the expressions 'presenile' dementia and 'senile' dementia which was unfortunate, insofar as it implied that cases with onset of disease before 60 years of age (presenile) had one disease called AD ,whereas cases with onset after 60 years of age (senile) had another disease called "senile dementia". It is now well accepted that, regardless of the age of onset, presenile and senile dementias are manifestation of one disease, i.e. AD. AD has also been called primary degenerative dementia. It is referred to as 'degenerative' because the brain cells wither away and die. This disrupts the production and distribution of certain chemicals called neurotransmitters that carry messages within the brain. Brain cells are not damaged from outside by conditions such as severe brain in-

jury, tumors or strokes which affect the brain. As there is no cause for the disease, it is referred to as a 'primary' disorder, which in medical terms implies "without cause".

3 Clinical Symptoms

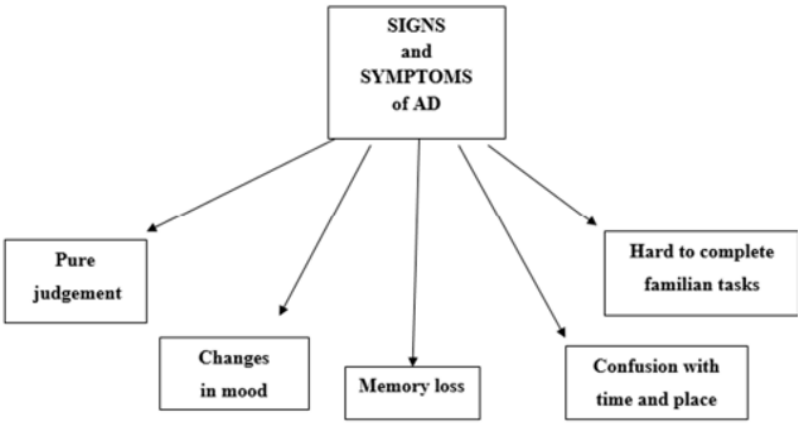


Figure 6.1. Early symptoms of AD
(Beata et al.,2023,p.2)

Burns and Iliffe (2009) revealed that memory loss is the primary symptom in most cases of Alzheimer's disease The gradual onset of memory loss means that it may (understandably) be misattributed to normal ageing and is often recognised only in retrospect as the onset of Alzheimer's disease. The onset is insidious, emerging with mild loss of memory and difficulty with word finding, symptoms that are common in everyday life to varying degrees. It is only when the symptoms interfere significantly with social and work activities, or are recognised by others, who sense they are progressing, that suspicion of a dementia is justified. Emotional changes are common, major depression occurs in 24-32% of cases, anxiety in 17-27%, apathy in up to 41%, and delusions in 23% The figure 6.2 displays the clinical features based on brain damage.

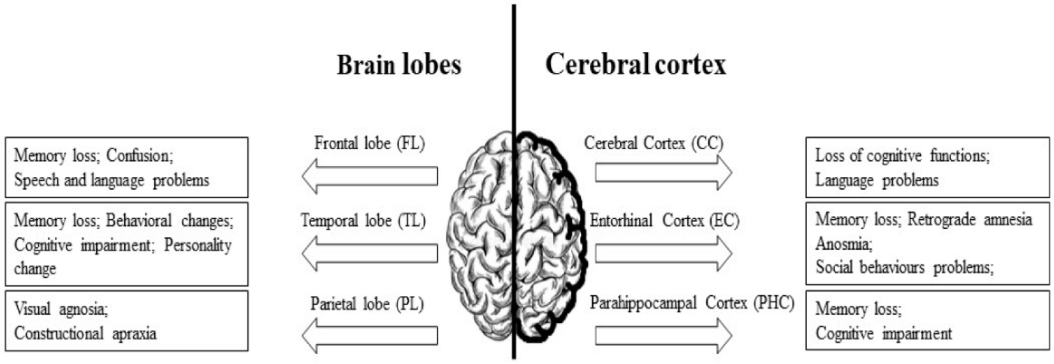


Figure 6.2. Effects of damage to individual parts of the brain throughout the course of AD (Beata et al .,2023,p.2)

4 Etiology of AD

Neurofibrillary tangles and aberrant neuritic plaques are hallmarks of Alzheimer's disease, a brain ailment that results in the death of neurons, particularly cholinergic ones. Numerous risk factors have been found, despite the fact that the precise cause is unknown. This section seeks to elucidate underlying mechanisms through a variety of hypotheses and risk factors.

4.1 Cholinergic and oxidative stress hypothesis

In the 1970s, neocortical and presynaptic cholinergic deficits were reported to be related to the enzyme choline acetyltransferase (ChAT), which is responsible for the synthesis of acetylcholine (ACh). Due to the essential role of ACh in cognitive function, a cholinergic hypothesis of AD was proposed. ACh is synthesized in the cytoplasm of cholinergic neurons from choline and acetyl-coenzyme A by the ChAT enzyme and transported to the synaptic vesicles by vesicular acetylcholine transporter (VAChT). In the brain, ACh is involved in several physiological processes such as memory, attention, sensory information, learning, and other critical functions. Degeneration of the cholinergic neu-

rons was found to take place in AD and to cause alternation in cognitive function and memory loss. B-amyloid is believed to affect cholinergic neurotransmission and to cause a reduction in the choline uptake and a release of ACh. Studies demonstrated that cholinergic synaptic loss and amyloid fibril formation are related to Aβ oligomers' neurotoxicity and to interactions between AChE and Aβ peptide. Additional factors also contribute to the progression of AD, such as a reduction in nicotinic and muscarinic (M2) Ach receptors, located on presynaptic cholinergic terminals, and the deficit in excitatory amino acid (EAA) neurotransmission, where glutamate concentration and D-aspartate uptake are significantly reduced in many cortical areas in AD brains. This is in addition to the use of cholinergic receptor antagonists such as scopolamine, which was found to induce amnesia. This effect can be reversed by using compounds that activate acetylcholine formation.(Breijyeh & Karaman ,2020,p. p4-5)

4.2 Aβ cascade and Tau hypothesis

The Aβ cascade hypothesis and the Tau hypothesis are two theories that suggest a relationship between the levels of a substance and its effects on its properties.

Pathogenesis of AD is better understood than other degenerative dementias. The primary culprits for AD are the accumulation of beta amyloid protein (called as amyloid plaques) outside the neurons and accumulation of tau protein (called tau tangles) inside the neurons. Physiologically, Aβ peptides are considered to play an important role in metal chelation, cholesterol transport, repair of blood vessels, and have an anti oxidant property. In normal states, amyloid precursor protein (APP) is the first cleaved by α secretase to an 83 amino acid peptide which is further cleaved by secretase into two smaller fragments viz., p7 and p3. However, in subjects with AD, APP is first cleaved by β secretase into a 91 amino acid peptide which is then cleaved by secretase into smaller Aβ40, Aβ42, or Aβ43 amino acid peptides. Among these, Aβ42 is specifically involved in the production of amyloid plaques. These Aβ42 peptides form

oligomers that interfere with synaptic functioning and action of neurotransmitters, particularly acetylcholine. Later, these oligomers further aggregate to form plaques. Formation of plaques leads to a series of inflammatory and biochemical reactions that result in hyperphosphorylation of tau proteins of microtubules. These tau proteins then aggregate to form neurofibrillary tangles. Accumulations of beta amyloid proteins disrupt the communication at the synapse between different neurons, whereas accumulation of tau proteins disrupts the inflow of nutrients and other essential molecules into the neurons. Together these plaques and tangles lead to neuronal death and gradual loss of cognitive functions(Grover and Somani,2016,p.102).

Amyloid and tau deposition progress spatiotemporally in a predictive manner. Amyloid first accumulates in the basal part of the frontal, temporal, and occipital lobes, and subsequently spreads to the entorhinal cortex, hippocampus, amygdala, insular cortex, and cingulate cortex, sparing the primary visual and sensorimotor cortices. Conversely, neurofibrillary tangle deposition progresses in the following order: transentorhinal cortex, entorhinal cortex, hippocampus, temporal cortex, association cortices, and finally the primary sensorimotor and visual cortices.(Park et al.,2016,p.828)

4.3 Inflammation hypothesis

Reactive gliosis and neuroinflammation are hallmarks of AD. Microglia-related pathways were considered to be central to AD risk and pathogenesis, as supported by emerging genetic and transcriptomic studies. Increasing evidence demonstrate that microglia emerges as central players in AD. In very early stage, microglia, TREM2 and complement system are responsible for synaptic pruning . The processes of activitydependent and long-term synaptic plasticity are the common and fundamental cellular underpinning of learning and memory which may manifest as influence on long term potential . Following that, reactive microglia and astrocytes will surround amyloid plaques and secrete numerous pro-inflammatory cytokines. These events are regarded as an early,

prime mover in AD evolution (Du et al.,2018,pp.6–7)

According to Abukuri,(2023) Neuroinflammation, a common cause of cognitive decline, can lead to disorders like Alzheimer's disease and dementia due to aging. Aβ, a proinflammatory molecule, is a major contributor to neurodegeneration in AD. Age increases inflammation, making it a major risk factor for cognitive decline. Studies suggest neuroinflammation influences or initiates AD pathogenesis, with mutations in microglial gene regulating microglial activity increasing the likelihood of developing AD. Neuroinflammation is associated with neuronal damage and cognitive impairment.

Genetic, cellular, and molecular changes associated with AD point to the involvement of immune and inflammatory processes. However, it is not yet known whether inflammation is a cause, contributor, or secondary phenomenon in AD . Microglia, the brain's resident macrophages, are pivotal players in immune/inflammatory response in multiple neurological disorders, including AD. They remove redundant, apoptotic neurons. They secrete a wide variety of inflammatory factors, including reactive oxygen species, T cell-1 cytokines, chemokines, growth factors, and complement components. These inflammatory factors are elevated in pathologically vulnerable regions of the AD brain. The dense accumulation of microglia within and around Aβ deposits suggests that aggregated Aβdeposits are potent stimuli for inflammatory responses. It is hypothesized that amyloid deposition is the primary event in Alzheimer pathogenesis. While this deposition is being dealt with by microglia in their phagocytic mode, there are few consequences (high amyloid controls). When the microglia become overwhelmed, they switch to inflammatory (cytokine production) mode, then neuronal toxicity and neurodegeneration are initiated.(Raskin et al.,2015,p.716)

4.4 New pathway to AD

AD is conventionally regarded as a central nervous system (CNS) disorder. However, increasing experimental, epidemiological and clinical evidences have suggested that

manifestations of AD extend beyond the brain. Most notably, research over the past few years reveals that the gut microbiome (GMB) has a profound impact on the formation of the blood-brain barrier, myelination, neurogenesis, and microglia maturation . In particular, results from germ-free animals and animals exposed to pathogenic microbial infections, antibiotics, probiotics, or fecal microbiota transplantation showed that gut microbiota modulates many aspects of animal behaviors, suggesting a role for the gut microbiota in host cognition or AD-related pathogenesis. The underlying mechanisms of gut microbiota influencing brain involve the communication through immune system, the endocrine system, the vague nerve, and the bacteria-derived metabolites.

4.4.1 Endocrine pathway and the vagus nerve

The gut is the largest endocrine organ in the body. Gut microbiota can regulate secretion of many hormones from intestinal endocrine cells, such as corticosterone and adrenal hormones, and thus establish the information exchange between the intestines and the brain. For example, the intestinal microbiome can affect the secretion of serotonin and regulate brain emotional activities ; intestinal microbial metabolism can also produce a variety of neurotransmitters, such as dopamine, GABA, acetylcholine and melatonin, which are transmitted to central nervous system through the vagus nerve . Besides transporting these signal substances, the vagus nerve itself plays an important role in inflammation and depression . The vagus nerve can influence the gastrointestinal tract, orchestrate the complex interactions between central and peripheral neural control mechanisms . The stimulation of vagus nerve is able to regulate mood, and the immune system, suggesting the therapeutic potential of vagus nerve modulation to attenuate the pathophysiological changes and restore homeostasis.(Du et al.,2018,p.p 6-7)

4.4.2 Bacteria-derived metabolites

According to Du et al.(2018),The gut microbiota plays a crucial role in generating essential nutrients for host physiology, and its metabolites, such as SCFAs, can modulate peripheral and central pathologic processes. The gut microbiota can secrete amyloids and lipopolysaccharides, which may contribute to the production of proinflammatory cytokines associated with Alzheimer's disease (AD). However, the theoretical basis for microbiota-directed therapies in neurodegenerative disorders still needs support from high-quality clinical trials. Recent research suggests an increase in pro-inflammatory GMB taxon and a reduction in antiinflammatory taxon may be associated with peripheral inflammatory states in patients with cognitive impairment and brain amyloidosis.

An interesting aspect is connected to iron dyshomeostasis. Many physiological processes in the human body depend on iron, yet as we age, iron is continuously stored in the brain. Early research discovered that Alzheimer's disease's cognitive deterioration isdirectly correlated with iron excess. What is more, both APP and tau protein are connected with iron metabolism . Iron participates in the creation of neurotransmitters, myelination, and antioxidant enzyme activity in the brain . It has been shown that having an excessive amount of iron speeds up the development of neurofibrillary tangles and senile plaques . What is more, a heavy iron diet can cause cognitive deterioration in mice,an increase in aberrant tau phosphorylation in neurons, and inappropriate production ofproteins associated with the insulin system. Supplemental insulin can lessen tau phosphorylation brought on by iron , proving that iron buildup may interfere with insulin signaling and cause tau hyperphosphorylation.(Doroszkiewicz & Mroczko,2022,p.3)

4.4.3 Immune pathway

Jorf et al.(2023), suggest that the brain and peripheral immune system interact via three routes : the BBB, choroid plexus (CP), and meninges. Changes in these CNS borders with advancing age could initiate disease pathology or exacerbate neuropathogenesis.

CP dysfunction exhibits fbrosis, an increase in type I interferons (IFN), and local neuroinflammation, while impaired CP transportation function reduces Aβ clearance in the AD brain. Evidence for T cell infiltration into the brain parenchyma through meningeal lymphatic vessels suggests a broader role for peripheral immune cells in both healthy and diseased brains.

Recent insights into the functions and communications between the glymphatic system and meningeal lymphatics in CNS disorders have recognized new important players in neurophysiology. Disturbances in glymphatic efflux due to sleep disorders or chronically impaired glymphatic system have been associated with neurodegenerative diseases such as AD. Reduction in meningeal lymphatic drainage has also been linked with aging-associated cognitive decline and an impaired glymphatic system to recirculate CSF through the brain. An aging-related deficit in C-C chemokine receptor type 7 (CCR7) contributes to a reduction in glymphatic efflux, cognition, and increased β-amyloid deposits in the brain of 5XFAD mice.

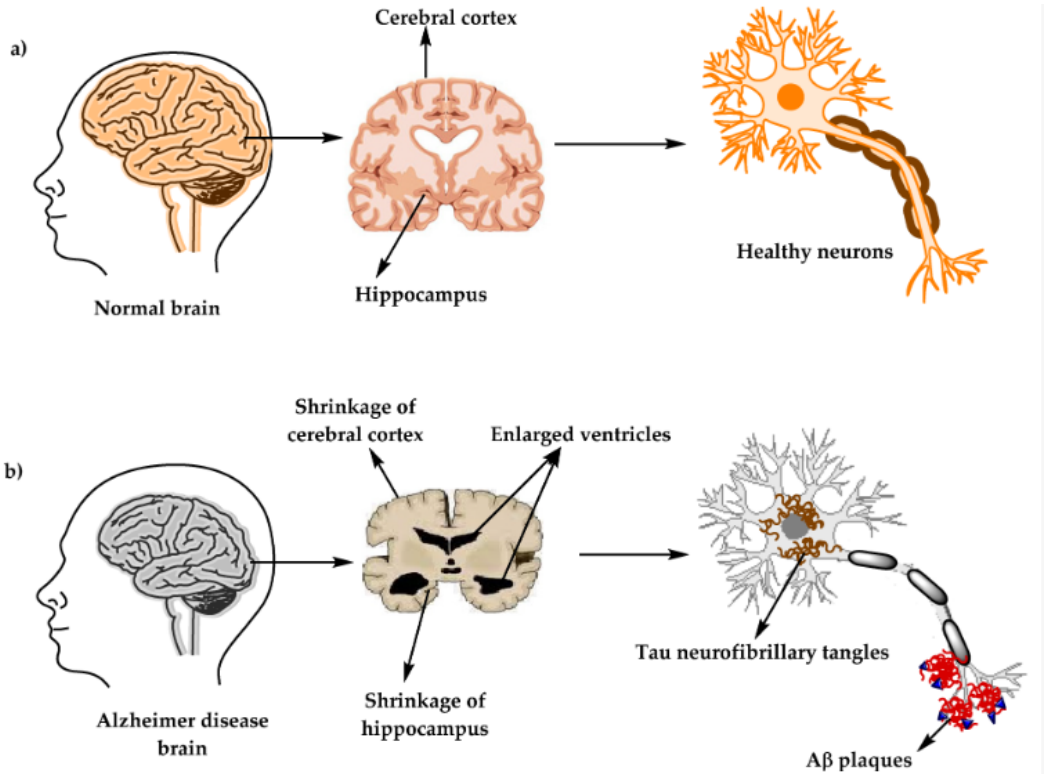


Figure 6.3. The physiological structure of the brain and neurones in (a) healthy brain and (b) alzheimer's disease brain

(Breijyeh & Karaman ,2020,p.2)

5 Psychological risk factors

A number of psychological factors, including personality traits and affective states, are related to Alzheimer's dementia, and investigators have explored the relationships between these factors and pathology. Conscientiousness—the tendency to be self-disciplined, scrupulous, and purposeful— showed no direct relationship with AD or other pathologies but modified the relationship between tangle density and infarcts with cognition . Harm avoidance, a personality trait indicative of behavioral inhibition (e.g., pessimism and shyness), was associated with infarcts but not with AD pathology . A sense of purpose in life has been strongly linked to a number of health outcomes in aging, in-

cluding dementia, and it appears to modify the association between AD pathology and cognition, implying a source of reserve . Finally, depressive symptomology is related to cognitive decline independent of pathology and does not appear to be the result of preclinical pathology, as some have posited.
Altogether, it appears that psychological factors may provide a reserve to cope with AD pathology and that some of these factors work through vascular mechanisms, but none are direct risk factors for AD.(James & Bennett, p.p 72-73)

6 Diagnosis of AD

A pathological analysis based on an autopsy is the gold standard for the diagnosis of Alzheimer's disease.The number and location of neurofibrillary tangles and amyloid plaques in the brain are used to stage the disease and determine the presence of definitive Alzheimer's disease. In clinical settings, the diagnosis of Alzheimer's disease is mostly made using the patient's medical history, physical, neurological examinations, and neuropsychological testing. Selected ancillary testing is also used to rule out other potential causes. In comparison to the pathological diagnosis, the clinical diagnosis of Alzheimer's disease has an accuracy of 70-90%, with higher accuracies being attained in specialized settings such as memory disorder. A set of consensus criteria first established in 1984. Most recently updated in 2011 by the National Institute on Aging and Alzheimer's are the corner stone of the clinical diagnosis. The diagnosis of possible Alzheimer's disease dementia is advised when the patient's cognitive impairment follows an unusual clinical course or suspected of being brought on by etiologies other than Alzheimer's disease. On physical and neurological exams, Alzheimer's disease patient's typically have normal results. Only for exploratory purposes or as a supplement to the clinical criteria for Alzheimer's disease are laboratory and neuroimaging techniques utilized, notably to rule out structural brain lesions and find it reversible dementia

causes. The American Academy of Neurology advises only the routine measurement of serum B12, thyroid stimulating hormone (TSH), free thyroxine (T4) levels as part of the workup for dementia to rule out cerebral hematomas, brain tumors, cerebrovascular lesions as well as normal pressure hydrocephalus, structural MRI or non-contrast computed tomography (CT) may be helpful.(Nivetha et al.,2023,p.383)

Conclusion

Aging is a complex process influenced by biological, psychological, social, and cultural factors. Understanding the psychological states of older adults is essential for addressing various mental health issues, such as dementia, alzheimer's disease, depression, and anxiety. Identifying normal and abnormal aging patterns requires recognizing the changes that occur during this stage, which helps in understanding and explaining pathological conditions.

Conclusion

Conclusion

Mental health disorders are complex conditions that greatly affect individuals and manifest through a range of symptoms and underlying mechanisms. Due to their complexity, many of these disorders remain underdiagnosed or misdiagnosed. To accurately understand disorders such as schizophrenia, obsessive-compulsive disorder and conversion disorder, it is necessary to consider neurobiological, psychological and social factors. In addition, clinicians must distinguish between normal aging and pathological conditions to ensure accurate diagnoses and timely interventions. Mastery of this unit is therefore essential for clinical psychology students as it provides them with knowledge and skills essential for clinical practice.

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