Anxiety and Anxiety Disorders

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Anxiety = Fear?

Similarities

- Negative affect, experienced as subjectively similar
- Accompanied by bodily sensations (elevated arousal)
- Elicited by the same triggers - response to a threat or danger
- Future-oriented: anticipation of danger/discomfort
Anxiety = Fear?

Differences (1)

- **Nature of threat**
  - Fear: known, identifiable, external, circumscribed, specific, immediate
  - Anxiety: unknown, elusive, internal, without clear boundaries, “located” in the future

- **Response to threat**
  - Fear: emergency (“fight or flight”)
  - Anxiety: vigilance
Anxiety = Fear?

Differences (2)

- **Onset**
  - Fear: clear-cut
  - Anxiety: less clear-cut, vague

- **Course**
  - Fear: acute, episodic
  - Anxiety: chronic, persistent

- **Quality of the experience**
  - Fear: rational
  - Anxiety: puzzling
Normal v Pathological Anxiety

Criteria for differentiation

- Intensity
- Quality of the experience
- Duration
- Context and appropriateness of response ("true alarms" v "false alarms")
- Negative effects on behaviour and functioning (impairment as a result of anxiety)
Anxiety Disorders: Main Features

- Pathological anxiety is the dominant emotional characteristic (but other emotions may also be prominent, e.g., disgust, shame, guilt, anger)
- No “organic” aetiology of anxiety
- Not substance-induced
- Absence of psychosis
Classification of Anxiety Disorders (Based on DSM)

- Panic disorder with and without agoraphobia
- Generalised anxiety disorder (GAD)
- Social anxiety disorder/social phobia (SAD)
- Specific (isolated) phobias
- Obsessive-compulsive disorder (OCD)
- Posttraumatic stress disorder (PTSD)
Panic Disorder With and Without Agoraphobia

“A prototypical anxiety disorder”
Panic Disorder Components

- Panic attacks + anticipatory anxiety
- If phobic avoidance not present: panic disorder without agoraphobia
- If phobic avoidance present: panic disorder with agoraphobia
Characteristics of Panic Attacks

- Sudden occurrence
- Several physical symptoms (usually symptoms of autonomic hyperactivity): cardiac, respiratory, dizziness/fainting feeling
- Psychological symptoms: fear of dying suddenly, fainting/collapsing or losing control Going mad, depersonalisation/derealisation
- Peak of an attack within 10 minutes
Characteristics of Anticipatory Anxiety

- Fear of another panic attack
- “Fear of fear”
- Fear of and/or preoccupation with the symptoms of panic attacks and/or their anticipated consequences:
  - Physical consequences (e.g., dying)
  - Psychological consequences (e.g., loss of control)
  - Social consequences (e.g., embarrassment, shame)
Characteristics of Phobic Avoidance in Panic Disorder

- Avoidance is panic-driven: the main purpose is to avoid/prevent panic attacks
- Agoraphobia = avoidance of situations in which, in case of a panic attack:
  - Escape might be difficult or embarrassing
  - Help might not be available
- Agoraphobia pertains to avoidance of several, often numerous situations
- Typical agoraphobic situations: crowded places, public transport, travelling far away from home, being alone, standing in a queue
Epidemiology of Panic Disorder

- Lifetime prevalence in different countries: 1.4-2.9% (except for Asian countries, where the lifetime prevalence rates are 0.4-1.5%)
- Male-to-female ratio: 1:1.5-2.5
- Male-to-female ratio if agoraphobia is present: 1:2.5-4
- Typical age of onset: third decade of life
- High prevalence in primary care, certain specialized medical settings (cardiology, otolaryngology, gastroenterology) and hospital emergency rooms
Course of Panic Disorder

**Recovery**  
- Complete or almost complete remission  
- No impairment in functioning  
- No need for treatment  

**30-35%**

**Chronic, with fluctuations**  
- Mild and/or occasional symptoms  
- Minor and/or occasional interference with functioning  
- Occasional, sometimes a prolonged need for treatment  

**50%**

**Chronic, without fluctuations**  
- Continuous and moderate to severe symptoms  
- Complications of panic disorder more likely  
- Continuous interference with functioning  
- Continuous need for treatment  

**15-20%**
Aetiology of Panic Disorder: Biological Factors (1)

- Abnormally sensitive anxiety-regulating mechanism originating in the amygdala lowers the “threshold” for tolerating sensory information, so that ordinary sensory information activates autonomic responses (through brain-stem nuclei) and the accompanying catastrophic cognitions (through the cortex), leading to a panic attack.

- Panic attacks can be artificially induced by increasing the respiration rate (hyperventilation), inhaling carbon dioxide or disrupting the acid-base balance.

- Acute hyperventilation leads to a panic attack via hypocapnia and alkalosis.
Aetiology of Panic Disorder: Biological Factors (2)

Panic attack as a consequence of:

- Hypersensitivity to carbon dioxide of the brain stem chemoreceptors
- Premature and inappropriate activation of the alarm mechanism, which aims to prevent choking (false suffocation alarm theory)
- Increased central noradrenergic activity (hypersensitivity of the presynaptic alpha-2 receptors, increased firing rate of the locus coeruleus)
- Failure of the GABA system to inhibit the locus coeruleus
Aetiology of Panic Disorder: Cognitive Factors

Common to all anxiety disorders:
- Exaggerated perception of threat and danger

Relatively specific for panic disorder:
- Threat is perceived to originate within one’s body
- Hypervigilance about physical sensations and bodily functioning
- Misinterpretation of physical sensations as a sign of an impending catastrophe
- Beliefs that anxiety and its (physical) symptoms are dangerous, leading to a fear of anxiety and its (physical) symptoms
Pharmacotherapy of Panic Disorder (1)

1\textsuperscript{st} line: SSRIs (especially paroxetine, sertraline, citalopram)
2\textsuperscript{nd} line: TCAs (clomipramine, imipramine)
3\textsuperscript{rd} line: SSRIs or TCAs + high-potency benzodiazepines (clonazepam, alprazolam); combination given for initial 6-8 weeks of treatment, followed by the treatment with SSRIs or TCAs only
4\textsuperscript{th} line: high-potency benzodiazepines only
Other agents: classical MAOIs, venlafaxine, mirtazapine, reboxetine
Pharmacotherapy of Panic Disorder (2)

- Duration of pharmacotherapy: at least 1 year after achieving remission
- Most common problems:
  - Increased anxiety, agitation, “jitteriness syndrome” at the beginning of treatment with SSRIs and TCAs
  - Slow onset of antipanic effect with SSRIs and TCAs (after 6-8 weeks of treatment)
  - Dependence in the course of long-term treatment with benzodiazepines
  - High relapse rates upon discontinuation of medication
Cognitive-Behavioural Therapy (CBT) for Panic Disorder

- Cognitive therapy (cognitive restructuring): changing threat and danger appraisals, correcting interpretations of physical sensations and symptoms, learning not to be afraid of anxiety/panic and its symptoms
- Behaviour therapy for agoraphobia: gradual, self-directed exposure in vivo to phobic situations, with decrease in anxiety occurring through habituation, extinction and enhanced sense of mastery
Generalised Anxiety Disorder (GAD)

“Anxiety disorder closest to normality”
Characteristics of GAD

- Pathological worry
- Symptoms of tension
- Various physical symptoms (less prominent than in panic disorder)
Pathological Worry in GAD

- Severe, excessive
- Constant or almost constant (present more often than not, most of the day, nearly every day), chronic
- Ruminative and uncontrollable (e.g., the person is unable to stop worrying); although it is self-initiated, it has an intrusive quality
- Relates to several “topics” or “domains” (e.g., the person worries about health, finances, relationships and work at the same time)
- Often pertains to remote future circumstances
Tension in GAD

- **Psychological aspects of tension**
  - Nervousness, feeling keyed up/on edge, unable to relax, “inner” restlessness, irritability, difficulty concentrating, hypervigilance, exaggerated startle response

- **Physical (somatic) aspects of tension**
  - Muscle tightness or stiffness (muscle tension): stiff neck, back pain, shoulder pain, tension headache; muscle spasms, tic-like movements, jerks, fine tremor, difficulty swallowing

- **Consequences of tension**
  - Sleep disturbance, agitation, fatigue, exhaustion
Epidemiology of GAD

- Lifetime prevalence in various countries, using various diagnostic criteria: 1.9-9.2%
- One of the most common psychiatric disorders in primary care
- Rarely occurs alone (usually co-occurs with depression, social anxiety disorder and panic disorder)
- Relatively high prevalence in all age groups
- Most common anxiety disorder among the children and the elderly
- Typical age of onset: 15-25
- Male-to-female ratio: 1:2
- Majority of persons with GAD do not seek help at all; long period between the onset of GAD and time of seeking help; help is usually sought in primary care for a disorder that complicates the course of GAD (e.g., depression)
Aetiological factors in GAD

- Genetic predisposition
- Other biological mechanisms unclear:
  - Hyperactivity of the noradrenaline system?
  - Decreased function of the GABA-A receptors?
- Cognitive models:
  - Worry as “cognitive avoidance” (worry serving the purpose of avoiding unpleasant somatic symptoms that accompany strong emotional states)
  - Beliefs about benefits of worry (worry being maintained by the beliefs that it is necessary to worry in order to avoid danger, prevent harm, prepare oneself for the bad outcome and/or promote better coping)
  - Interpretation of a wide variety of ambiguous stimuli and information as threatening
Pharmacotherapy of GAD

1\textsuperscript{st} line: venlafaxine, SSRIs (especially paroxetine, sertraline)
2\textsuperscript{nd} line: TCAs (imipramine) or trazodone
3\textsuperscript{rd} line: venlafaxine, an SSRI or a TCA + benzodiazepine; combination given for initial 6-8 weeks of treatment, followed by the treatment with venlafaxine, an SSRI or a TCA only
4\textsuperscript{th} line: buspirone
5\textsuperscript{th} line: hydroxyzine
CBT for GAD

- Behaviour therapy techniques: progressive muscle relaxation and other means of controlling the symptoms of anxiety and tension
- Cognitive restructuring:
  - Improving “problem orientation” (correcting steps in the decision-making and problem-solving processes, coping better with uncertainty)
  - Cognitive exposure (imagery exposure to the content of worries)
  - Identifying specific beliefs about the benefit of worrying + challenging these beliefs
Social Anxiety Disorder (SAD)

“Not just extreme shyness”
Clinical Features of SAD

- Excessive and persistent fear of:
  - Performance-type situations ("performance anxiety"), e.g., speaking in public, eating or writing in front of others, performing work duties under observation, using public toilets in the presence of others
  - Social interactional situations, e.g., interpersonal communication (formal and informal), speaking with authority figures, asking for directions, returning purchased goods, expressing an opinion
- This fear leads to avoidance of social situations or to their endurance with a lot of anxiety or distress
Underlying Fears in SAD

- Fear of negative evaluation
- Fear of being under scrutiny
- Fear of making a mistake
- Fear of having visible physical symptoms that would reveal anxiety
- Anticipation of the interference with performance or of generally performing poorly
Subtypes of SAD

- Nongeneralised SAD
  - Fear of one or just a few social situations (usually performance-type situations)

- Generalised SAD
  - Fear of numerous social situations (both performance-type and interactional social situations)
Epidemiology of SAD

- Lifetime prevalence rates quite different in different countries, also differ according to the diagnostic criteria used (e.g., 2.7-13.3% in the USA)
- Male-to-female ratio: F>M in the community; F=M in clinical settings
- More likely to be single, unemployed, in the lower socio-economic group, with lower levels of education (=consequence of SAD)
- Age of onset: usually in adolescence (mid-teens to early 20s)
- Usual period between onset and time of seeking help: >10 years
Aetiological Factors in SAD

- Genetic predisposition
- Behavioural inhibition to the unfamiliar, as a temporally stable component of inborn temperament: observable during the 1\textsuperscript{st} year of life and manifesting as difficulty sleeping in unfamiliar surroundings, irritability in novel situations, avoidance of contacts with unfamiliar people, places and objects, etc.
- Cognitive models: SAD results from an expectation to be evaluated negatively in social situations, with such an expectation being a consequence of certain assumptions and beliefs about oneself and others
Pharmacotherapy of SAD (1)

- Pharmacological approach depends on whether the patient has a nongeneralised or generalised type of SAD.
- Choice of medication largely depends on whether there is a co-occurring depression or alcohol abuse/dependence.
- Great caution when benzodiazepines are administered to patients with SAD, as there is higher risk for alcohol and other substance abuse in these patients than in patients with other anxiety disorders.
Pharmacotherapy of SAD (2)

Generalised type of SAD
- 1\textsuperscript{st} line: SSRIs (especially paroxetine, sertraline)
- 2\textsuperscript{nd} line: classical, irreversible MAOIs
- 3\textsuperscript{rd} line: benzodiazepines (clonazepam)

Nongeneralised type of SAD
- 1\textsuperscript{st} line: beta-adrenergic blockers (propranolol, atenolol)
- 2\textsuperscript{nd} line: benzodiazepines
CBT for SAD

- Exposure: technique that should always be used, because of its efficacy
- Social skills training: technique that should be used if there is a marked deficit in social skills
- Cognitive restructuring: technique that should be used with the goal of directly making relevant cognitive changes (e.g., correcting self-appraisals, normalising interpretations in relevant social situations)
- Exposure + social skills training or exposure + cognitive therapy or exposure + cognitive therapy + social skills training: for enhancement of treatment effects and/or achievement of multiple treatment goals
Specific Phobias

“So widespread, yet rare in clinical settings”
General Characteristics of Phobias

- Fear of known objects, situations, activities or phenomena (“phobic stimuli”)
- Phobic stimuli generally do not pose a realistic threat; if they do, the anxiety response is irrational or excessive
- There is an insight that the fear is irrational or excessive
- Exposure to phobic stimuli elicits an immediate anxiety response
- There is avoidance of phobic stimuli or endurance of phobic stimuli with great distress and/or anxiety
- There is an impaired functioning or significant distress about having the fear
Types of Specific Phobias

- Animal phobias
- Blood-injection-injury phobia
- Situational phobias
  - Fear of enclosed places (claustrophobia)
  - Driving phobia
  - Fear of flying
- Natural environment type
  - Fear of heights (acrophobia)
  - Water phobia
- Other phobias
  - Illness phobia
  - Fear of choking/vomiting
Epidemiology of Specific Phobias

- Prevalence rates likely to be different in different countries; lifetime prevalence in the USA: 11.3-12.5%
- Generally more common among women (except for the blood-injection-injury phobia), with a male-to-female ratio of 1:2-2.5
- Usual age of onset depends on the phobia subtype:
  - Animal phobias: (early) childhood
  - Blood-injection-injury phobia: (later) childhood
  - Situational phobias: adolescence, early 20s
  - Natural environment subtype of phobias: variable
- Very few persons with specific phobias seek professional help and treatment
Aetiological Factors in Specific Phobias

- Genetic predisposition (especially for blood-injection-injury phobia)
- Acquisition through learning:
  - Traumatic conditioning (direct aversive experience with the phobic stimulus)
  - Vicarious learning (observation of the fear in others)
  - Transmission of the relevant information (e.g., information on dangerousness of certain objects or situations)
- “Innate” fears (not a product of learning; fears with “evolutionary”/survival value)
Treatment of Specific Phobias

- Various techniques of behaviour therapy, based on exposure, are most effective
- Exposure:
  - Gradual v flooding
  - Imaginal v in vivo
  - Self-directed v therapist-assisted
Obsessive-Compulsive Disorder (OCD)

“Most intriguing of all disorders”
Characteristics of Obsessions

- Thoughts, impulses and/or images
- Recurrent/repetitive
- Uncontrollable
- Not just excessive worries about real-life problems
- Cause marked anxiety or distress
- Usually (though not invariably) experienced as alien, intrusive, strange, “crazy”, senseless, inappropriate and/or portending harm
- Compel the person to attempt to ignore, suppress or neutralize obsessions or resist them in some other way; this is with the purpose of:
  - Alleviating anxiety or distress
  - “Undoing” obsessions because of their alien or “dangerous” nature and/or
  - Preventing harm associated with obsessions
Common Types of Obsessions

Frequency (Rasmussen and Eisen, 1992)

- Multiple obsessions: 72%
- Contamination: 50%
- Pathological doubt: 42%
- Somatic: 33%
- Need for symmetry: 32%
- Aggressive: 31%
- Sexual: 24%
Characteristics of Compulsions

- Overt behaviours or unobservable mental acts (covert/mental/cognitive compulsions) that the person feels driven to perform in response to an obsession and often according to strict rules
- Repetitive
- Compulsions are performed with one or more of the following goals:
  - Alleviation of anxiety or distress that is caused by obsession (but compulsions are performed excessively and repeatedly, without achieving this goal in the long-run)
  - “Undoing” of obsession (although compulsions cannot realistically do that)
  - Prevention of harm associated with the obsession (although compulsions cannot realistically do that)
Common Types of Compulsions

Frequency (Rasmussen and Eisen, 1992)

- Checking: 61%
- Multiple compulsions: 58%
- Washing, cleaning: 50%
- Counting: 36%
- Need to ask or confess: 34%
- Need for symmetry or precision, rearranging objects: 28%
- Hoarding: 18%
Components of OCD

Obsessions
- Causing anxiety or distress and/or
- Experienced as alien and/or harm-portending

Neutralization
- Alleviating anxiety or distress and/or
- “Undoing” obsessions and/or
- Preventing harm associated with obsessions

BEHAVIOURAL
1. Overt compulsions
2. Avoidance
3. Reassurance seeking

MENTAL (COGNITIVE)
1. Covert (mental, cognitive) compulsions
Epidemiology of OCD

- Similar prevalence in different countries (lifetime prevalence rate between 1.5% and 2%)
- Male-to-female ratio: 1:1
- Age of onset earlier in males
- OCD in children and adolescents more common among males
- Mean age of onset: 21-22 years, with substantial proportion having an onset in childhood
- Average period between onset and time of seeking help: 7.5 years
Course of OCD

- Lasting remission or recovery: max 20%
- Fluctuating chronic course, with exacerbations and periods of complete or partial remission: 2-47%
- Steady (constant, continuing) chronic course, without significant fluctuations (no clear-cut exacerbations and remissions): 15-61%
- Progressive, deteriorating course: 5-14%
Aetiology of OCD: Biological Factors

- Dysfunction of the serotonin neurotransmitter system
- Increased dopaminergic function in some OCD patients, particularly those with the co-occurring tic disorders
- Implicated brain structures:
  - Limbic system: orbitofrontal cortex, cingulate, amygdala, thalamus
  - Basal ganglia: striatum (caudate nuclei)
- Dysfunction in the orbitofrontal (limbic)-basal ganglia circuits or cortico-striato-thalamo-cortical circuits
- Certain forms of OCD in childhood (co-occurring with Sydenham’s chorea or tics): autoimmune process after an infection with group A beta-haemolytic streptococci
Pharmacotherapy of OCD – Special Considerations

- Only medications with specific serotonergic effects (clomipramine, SSRIs) have been efficacious in OCD.
- Criteria for response to medications are less strict for OCD than for other anxiety disorders; as a result, many responders to pharmacotherapy are still quite symptomatic.
- Even with the less stringent criteria for response, only 40-60% of patients with OCD respond to clomipramine or SSRIs.
- Longer duration of treatment (at least 12 weeks) and higher doses of medications (usually higher than doses used in the treatment of depression) are needed for response to occur.
- Slow and gradual response to pharmacotherapy over weeks and months is often observed.
Choice of Medication in OCD

1\textsuperscript{st} line: SSRIs (especially fluoxetine, fluvoxamine, sertraline, paroxetine)

2\textsuperscript{nd} line: another SSRI (if no response at all to the first SSRI)

3\textsuperscript{rd} line: clomipramine (if no response at all to the two SSRIs)

Augmentations and combinations in case of partial response to 1\textsuperscript{st}, 2\textsuperscript{nd} or 3\textsuperscript{rd} line pharmacotherapy:

– SSRI or clomipramine + antipsychotic
– SSRI + clomipramine
– SSRI or clomipramine + clonazepam
CBT for OCD

- Behaviour therapy: exposure (to the obsession- and compulsion-related cues) and response prevention (abstaining from performing the compulsion)
- Cognitive restructuring: addressing responsibility appraisals (beliefs that patients are responsible for having obsessions) and faulty risk assessment (beliefs that having certain repugnant thoughts is the same as acting in accordance with such thoughts)
Posttraumatic Stress Disorder (PTSD)

“One of the most controversial disorders”
Development of PTSD

Unexpected/unpredictable event involving possible or actual death or serious injury (potential or real threat to one’s own life or life of others)

↓

Appraisal of the meaning and/or consequences of the event

↓

Reaction to the event: intense fear, helplessness, horror, other emotions (e.g., shame, guilt)

↓

Long-lasting impact of the event

↓

PTSD
Examples of Traumatic Events That May Precede PTSD

- Combat-related experiences
- Torture and other experiences of political prisoners, prisoners of war and concentration camp survivors
- Sexual assault
- Physical assault
- Sexual and physical abuse in childhood
- Armed robbery, other violent crime
- Road traffic accidents, other “man-made” accidents
- Natural disasters
Clinical Features of PTSD

- 3 groups of symptoms
  - Reexperiencing of the trauma (e.g., through nightmares and intrusive memories)
  - Avoidance of stimuli associated with the trauma (e.g., avoidance of activities or thoughts that arouse recollections of the trauma) and numbing of general responsiveness (e.g., markedly diminished interest, detachment from others)
  - Increased arousal (e.g., insomnia, hypervigilance, irritability)
Epidemiology of PTSD

- Prevalence rates of PTSD should be considered in conjunction with the trauma exposure rates, as the latter vary significantly in different populations.
- Lifetime prevalence rate in general population in the USA: 7.8%.
- Prevalence in victims/survivors of various traumas depend on the type of trauma (generally higher for combat-related trauma and in victims of assault and violence).
- Women are 2 times more likely to develop PTSD than men, even when controlling for exposure to traumatic events and type of trauma.
Course of PTSD

Recovery
- Tendency to spontaneously diminish in intensity and disappear in a substantial number of patients within a few years of its onset
- Recovery rates decrease sharply after PTSD has become chronic, and in particular, 1-2 years after its onset
- Recovery rate 5 years after the onset of PTSD: 18%

Fluctuating course (exacerbations and partial remissions)

Chronic, deteriorating course, often with complications (depression, substance abuse/dependence, enduring personality change) and lasting impairment in most areas of functioning
Aetiology of PTSD

Trauma is a necessary, but not a sufficient factor, for PTSD to develop
Risk Factors for Developing PTSD (1)

- **Demographics**: female gender
- **Family history**: family history of mental disorder, including PTSD, anxiety and antisocial behaviour
- **Childhood-related and developmental factors**: unstable family atmosphere, disrupted parent-child attachments, early separation from parents, physical and sexual abuse in childhood, behavioural disturbance and mental disorders during childhood (e.g., conduct disorder)
- **Psychopathology**: general psychological problems and psychiatric disorders (e.g., neuroticism, emotional immaturity, personality disorders, depression, anxiety disorders)
Risk Factors for Developing PTSD (2)

- **Clinical factors:** acute stress disorder, early development of PTSD-like symptoms, emotional numbing early after trauma, prominent avoidance, dissociation symptoms, depressive symptoms, severe physical consequences of the trauma (e.g., injuries, chronic pain), poor coping/adjustment/problem-solving skills

- **Social and environmental factors:** low level of social and/or family support, unfavourable/stressful life situation, subsequent exposure to the reactivating environmental factors, being a refugee, being separated from family/relatives/friends

- **Biological factors:** lower cortisol level and higher heart rate shortly after trauma (within the first week)

- **Cognitive factors:** excessively negative appraisals of the trauma, its consequences, oneself, responses of other people to the trauma, and the future; memory disturbances
Aetiology of PTSD: Biological Factors

- Hypersensitivity of the hypothalamic-pituitary-adrenal (HPA) axis to stress:
  - Abnormally low secretion of cortisol in response to stress, with the subsequently decreased levels of cortisol
  - Increased negative feedback regulation of cortisol

- Decreased hippocampal volume on the MRI scans

- PET findings on exposure to stress/reminders of the trauma:
  - Excessive activation of the limbic and perlimbic structures
  - Activation of the visual cortex
  - Decreased activity of the cortical areas involved in language expression
Classes of Medications Used in PTSD

- Antidepressants (SSRIs, TCAs, nefazodone, classical MAOIs)
- Noradrenergic suppressors (clonidine, propranolol)
- Mood stabilizers and anticonvulsants (lithium, carbamazepine, valproate, lamotrigine)
- Second-generation antipsychotics (risperidone, olanzapine, quetiapine)
- Non-benzodiazepine hypnotics (zolpidem, zopiclone, zaleplon)
- Benzodiazepines
Choice of Medication in PTSD

- **1st line:** SSRIs (especially sertraline and paroxetine)
- **2nd line:** nefazodone or TCAs (imipramine, amitriptyline), if no response at all to an SSRI
- **3rd line:** classical MAOI (phenelzine), if no response at all to the 1st or 2nd line medication

Augmentations and combinations in case of partial response to the 1st or 2nd line pharmacotherapy:
  - With noradrenergic suppressors
  - With mood stabilizers and anticonvulsants
  - With non-benzodiazepine hypnotics
  - With benzodiazepines
  - With second-generation antipsychotics
Psychotherapy of PTSD

- Techniques of CBT:
  - Exposure (gradual; imaginal, followed by in vivo exposure) to various aspects of the trauma
  - Cognitive restructuring: changing the manner in which patients appraise the trauma, their reactions to trauma, and the surrounding world

- Supportive psychotherapy

- Psychodynamic psychotherapy