Panic Disorder: Etiology, Clinical Features & Management

Outline

- Introduction
- History
- Epidemiology
- Etiology
- Clinical features
- Diagnostic criteria
- Differential diagnosis
- Management
- Summary

Introduction

- Fear and anxiety – 2 key core –ve emotions
- **Fear:** specific set of emotions/brain states elicited in an organism on confronting danger
- **Anxiety:** feeling of apprehension caused by anticipation of danger, may be internal or external
- **Fear:** acute response to proximal threats
- **Anxiety:** response to distal threats.

Introduction

- **Panic attack:**

  A period of intense fear characterised by a constellation of symptoms that develop rapidly, reach a peak of intensity in about 10 mins, and generally do not last longer than 20-30 mins (rarely over 1 hr). Attacks may be either spontaneous or situational.

- **Panic disorder:**

  Recurrent panic attacks, which are not secondary to substance misuse, medical conditions, or another psychiatric disorder.

History

- Panic - Greek god Pan, god of flocks, known for suddenly frightening animals and humans “out of the blue”
- 400 BC – Hippocrates – phobic avoidance
- 18th century - Jacob Mendes DaCosta – noted “irritable heart syndrome” in soldiers in the American Civil War – psychological & somatic symptoms
- 1870s – Benedikt – described individuals developing sudden anxiety and dizziness in public places

History

- 1895 - Sigmund Freud - anxiety neurosis - acute and chronic psychological and somatic symptoms
- Mid 1960s – Donald Klein – panic syndrome, responsive to imipramine
- Issac Marks – panic attacks and agoraphobic avoidance, responsive to behaviour therapy
- 1980 - Panic disorder 1st coined in DSM-III
- 1980-1994: close association with agoraphobia

Epidemiology

- Lifetime prevalence: 5%
- F:M = 2-3:1
- Mean age of presentation: 25 yrs.
- Lifetime prevalence of agoraphobia: 2-6%
- 75% of agoraphobic pts. - have panic disorder
- 91% panic disorder pts. & 84% agoraphobia pts. have one other psychiatric disorder
- 33% pts – MDD before onset
- Anxiety disorders common

Comorbidities

- 15-30% - Social phobia
- 2-20% - Specific phobia
- 15-30% - GAD
- 2-10% - PTSD
- 30% - OCD

Etiology

- Biological Factors – abn. regulation of brain noradrenergic (NA) systems
- CNS & PNS dysregulation
- ANS – increased sympathetic tone, adapts slowly to repeated stimuli, excessive response to moderate stimuli
- Neurotransmitters involved: NE, serotonin & GABA

Etiology

- NE – catecholamine released from locus ceruleus of pons
- Regulates body's behavioral & physiological response to stress
- Attenuation of local inhibitory GABAergic transmission in basolateral amygdala, midbrain and hypothalamus – anxiety-like physiological responses

Etiology

- In the panic disorder patients, including those who also had depression, receptors were reduced by an average of nearly one third in the anterior cingulate in the front middle part of the brain, the posterior cingulate, the rear middle part of the brain, and the raphe, as well as in the midbrain.

Etiology

- Panic-inducing substances (panicogens) – induce panic attacks in
  - most patients with panic disorder
  - much smaller proportion of persons without panic disorder or history of panic attacks.
- CO_2 (5-35% mix), sodium lactate, bicarbonate
- Directly affect NA, serotonergic & GABA receptors

Etiology

Temperamental:

- Negative affectivity and anxiety sensitivity
- History of "fearful spells" – risk factor for later panic attacks and disorder

Environmental:

- Childhood physical & sexual abuse
- Smoking
- Stressors

Brain Imaging

Structural neuroimaging: (MRI)

- Pathological involvement in temporal lobes, esp. hippocampus and amygdala.
- Cortical atrophy in right temporal lobe

Functional neuroimaging: (PET)

- Dysregulation (small increase or decrease) of cerebral blood flow
- a/w cerebral vasoconstriction – CNS S_X – dizziness

Genetic

- Distinct genetic component
- Panic disorder + agoraphobia – severe form, likely inherited
- 1st degree relatives – 4-8 times higher risk for panic disorder
- Twin studies: concordance: MZ > DZ

Clinical Features

- **Panic attack:** episode of abrupt intense fear accompanied by ≥ 4 of the autonomic/cognitive symptoms:

1. Palpitations, pounding heart, or accelerated heart rate
2. Sweating
3. Trembling/shaking
4. Sensations of shortness of breath or smothering
5. Feeling of choking
6. Chest pain or discomfort

Clinical Features

7. Nausea or abdominal distress
8. Feeling dizzy, unsteady, lightheaded, or faint
9. Derealization (feelings of unreality) or depersonalization (being detached from oneself)
10. Fear of losing control or going crazy
11. Fear of dying
12. Paresthesias
13. Chills or hot flashes

Clinical Features

- 1st attack - completely spontaneous
- Triggers: excitement, physical exertion, sexual activity, or moderate emotional trauma.
- Begins with 10-minute period of rapidly increasing symptoms (extreme fear + sense of impending death & doom)
- Pts. try to leave whatever situation they are in to seek help
- Duration: 20-30 mins, rarely > 1hr.
- Depression/depersonalization during attack

Clinical Features

- S_X disappear quickly/gradually
- Anticipatory anxiety between attacks about having another attack
- Somatic concerns of death from cardiac/respiratory problem
- Agoraphobia:
  - Rigidly avoid situations where obtaining help is difficult
  - Prefer being accompanied in busy streets, crowded stores, closed-in spaces/vehicles

Diagnosis

DSM-IV-TR: (Panic Disorder with or without Agoraphobia)

- Diagnostic criteria for panic disorder similar to DSM-5
- Agoraphobia - not a codable disorder
- Panic Disorder with Agoraphobia (300.21); Agoraphobia without History of Panic Disorder
- DSM-5 identifies agoraphobia as a separate diagnosis rather than a specifier

Diagnosis

DSM-IV-TR: (Agoraphobia Without History of Panic Disorder)

A. Agoraphobia related to fear of developing panic-like symptoms
B. Criteria for Panic disorder never met
C. Not attributable to the physiological effects of a substance/medical condition
D. If associated general medical condition is present, fear described in Criterion A is clearly in excess of that usually associated with the condition.

Diagnosis

DSM-IV-TR: (Agoraphobia)

A. Anxiety about being in places or situations from which escape might be difficult (or embarrassing) or in which help may not be available in the event of having an unexpected or situationally predisposed Panic Attack or panic-like symptoms.

B. Situations avoided/endured with marked distress/anxiety about having a Panic Attack or panic-like symptoms, or require the presence of a companion.

C. Not better accounted for by another mental disorder

Diagnosis

DSM-5: Panic Disorder

A. Recurrent unexpected panic attacks.

B. Atleast one of the attacks followed by ≥ 1 month of one or both:
   1. Persistent concern/worry about additional attacks
   2. Significant maladaptive behaviour related to the attacks

C. Not attributable to the physiological effects of a substance/medical condition

D. Not better explained by another mental disorder.

Diagnosis

ICD-10:

- Several severe attacks of autonomic anxiety within 1 month:
    1. In circumstances where there is no objective danger
    2. Without being confined to known/predictable situations
    3. With comparative freedom from anxiety symptoms in between attacks

Diagnosis

ICD-11: (6B01)

- Recurrent unexpected panic attacks not restricted to particular stimuli or situations.
- Discrete episodes of intense fear or apprehension with rapid and concurrent onset of symptoms (palpitations/increased heart rate, sweating, trembling, shortness of breath, chest pain, dizziness/lightheadedness, chills, hot flushes, fear of imminent death)

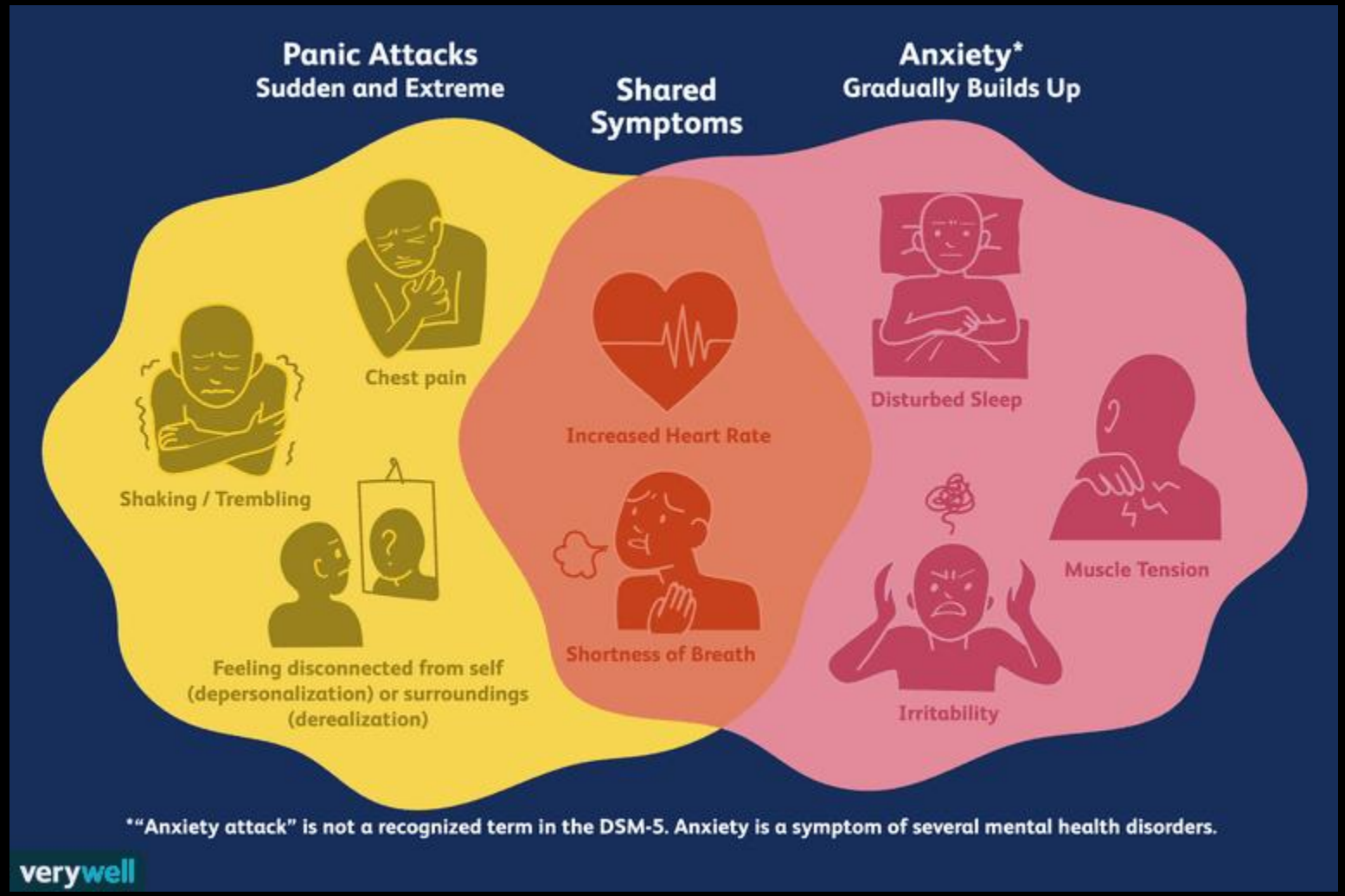
Diagnosis

ICD-11: (6B01)

- Persistent concern about recurrence/significance of panic attacks, or behaviors intended to avoid their recurrence, causing socio-occupational impairment.
- Not a manifestation of another health condition
- Not due to substance/CNS medication

- ***Excludes Panic Attack (MB23.H)*** – discrete episode

Clinical Features



Differential Diagnosis

Medical disorders:

- **CVS:** HTN, angina, MVP, CHF, MI
- **Respiratory:** asthma, pulmonary embolus, hyperventilation
- **CNS:** CVD, migraine, epilepsy, MS, Huntington's disease
- **Endocrine:** Addison's disease, hypoglycaemia, carcinoid syndrome, hypoparathyroidism, Cushing's syndrome
- **Drug intoxication:** amphetamine, hallucinogens, amyl nitrite, marijuana

Differential Diagnosis

Medical disorders:

- **Drug withdrawal:** alcohol, opioids, antihypertensives, sedatives-hypnotics
- **Others:** anaphylaxis, systemic infections, vit. B12 deficiency, SLE, electrolyte imbalance, heavy metal poisoning

Mental disorders:

- Anxiety disorders: social & specific phobia, PTSD, OCD
- GAD
- Agoraphobia without H/o panic disorder

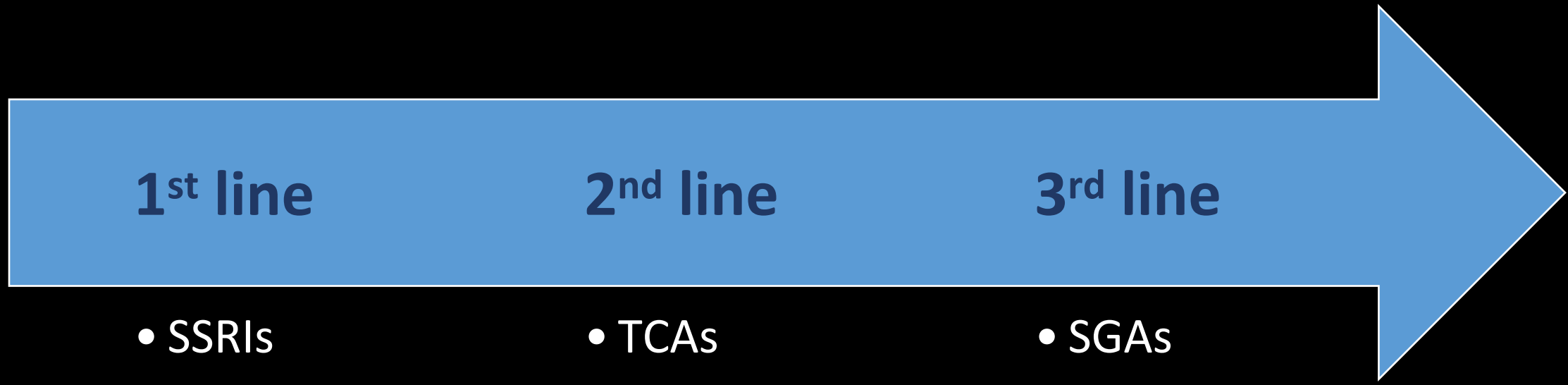
Course & Prognosis

- Chronic, variable course
- 30-40% - Sx free at long term follow-up
- 50%: mild Sx, doesn’t significantly affect
- 10-20%: significant Sx
- 40-80%: comorbid depression; may complicate
- 20-40%: alcohol & other substance dependence, OCD
- Agoraphobia thought to be caused by panic disorder – improves when panic disorder treated

Treatment

- Pharmacotherapy
- Cognitive Behavioral Therapy

Treatment


1st line
2nd line
3rd line
• SSRIs
• SNRIs
• TCAs
• MAOIs
• BZDs
• Others
• SGAs
• Anticonvulsants

Treatment

1st line

1. SSRI (fluoxetine, paroxetine, sertraline, escitalopram, citalopram)
2. SNRI (venlafaxine)

* - US-FDA approved

Treatment

SSRIs & SNRIs

- All SSRIs equally efficacious, differ in A/E (weight gain and discontinuation symptoms), drug interactions
- Choice made on:
  - Effectiveness & tolerance of A/E
  - Patient preference, past history of treatment response, costs & availability

Treatment

SSRIs & SNRIs

- Antidepressants take 4-6 weeks to become effective
- BZDs begin working within 1st week
- Antidepressants + BZD – speeds up therapeutic response
- Antidepressants - low and slow (avoid hyperstimulation reaction)
- BZDs – do not cause initial activation; difficult to taper & discontinue
- Venlafaxine: panic disorder + depression

Treatment

Class	Advantages	Disadvantages
SSRIs	Well-tolerated Safe in overdose Little weight gain Once-daily dosing	Initial activation Nausea, headache Insomnia initially Sexual side effects
SNRIs	Similar to SSRIs	Hypertension

Treatment

Class	Drug	Starting dose (mg/day)	Therapeutic range (mg/day)
SSRIs			
	Paroxetine	10-12.5 CR	10-40
	Fluoxetine	2.5-10	10-20
	Sertraline	25	50-200
	Citalopram	10	20-30
	Escitalopram	5	5-10
	Fluvoxamine	50	100-300
SNRIs			
	Venlafaxine	37.5	75-225

Treatment

2nd line

1. TCAs (clomipramine, imipramine)
2. MAOIs (phenelzine, tranylcypromine)
3. BZD (alprazolam, lorazepam, diazepam, clonazepam)
4. Others (mirtazapine, bupropion, reboxetine, inositol, buspirone)

Treatment

TCAs

- 1st drug – imipramine
- Clomipramine > imipramine
- Poorer tolerability

Treatment

Class	Advantages	Disadvantages
TCAs	Single daily dose Less expensive Long experience Antidepressant	Initial activation Anticholinergic A/E Weight gain Orthostatic hypotension Dangerous in overdose Sexual dysfunction

Treatment

Class	Drug	Starting dose (mg/day)	Therapeutic range (mg/day)
TCAs	**TID or QID**		**Acute total daily dose**
	Clomipramine	25	25-150
	Imipramine	10	50-200

Treatment

MAOIs

- Equal efficacy but several A/E
- Only one trial supporting its use
- Several A/E and tyramine diet requirement – limited use

Treatment

Class	Advantages	Disadvantages
MAOIs	More effective against comorbid depression Antidepressant	Dietary restrictions Hypertensive crisis (rare) Initial activation Insomnia Onset delayed Anticholinergic A/E Orthostatic hypotension Dangerous in overdose

Treatment

Class	Drug	Starting dose (mg/day)	Therapeutic range (mg/day)
MAOIs			
	Phenelzine	15	15-45 (or 90)
	Tranylcypromine	10	10-40 (or 70)

Treatment

BZDs

- Alprazolam – most widely studied
- Comparable to imipramine, better tolerated
- A/E – sedation, ataxia, slurred speech, memory complaints, dependency and recreational abuse

* - US-FDA approved

Treatment

BZDs

- Difficult to discontinue, abrupt discontinuation causes distress than gradual taper
- Dependence risk
- Short-term therapy to reduce/prevent panic attacks & reduce anticipatory anxiety
- Long term treatment doses comparable to short term or even lower

Treatment

Class	Advantages	Disadvantages
BZDs	Rapid efficacy Reduce anticipatory anxiety Well tolerated No initial activation Safe in overdose	Sedation Memory problems Withdrawal Abuse potential Rare sexual dysfunction

Treatment

Class	Drug	Starting dose (mg/day)	Therapeutic range (mg/day)
BZDs	**BID**		
	Alprazolam	0.25-0.5	2-10
	Clonazepam	0.25-0.5	1-4
	Lorazepam	0.5	1-7
	Diazepam	5	5-40

Treatment

3rd line

- Atypical antipsychotics
  - Preliminary evidence of benefit
  - Used in partial/no response
- Anticonvulsants (valproate, levetiracetam)

Treatment

- SSRIs + BZDs: Rapid control of severe symptoms
- Continue treatment for ≥ 6 months – continued improvement, decreased risk of relapse and recurrence
- Continue: ≥ 12-18 months; discontinuation - recurrence
- One SSRI fails – switch to another SSRI or switch to another class
- Fails – SGAs (Olanzapine, Risperidone)
- Maintenance: BZDs (alprazolam, clonazepam)
- Discontinuation done very gradually, esp. BZD

Treatment

Cognitive Behavioural Therapy

- Maybe superior to pharmacotherapy alone; cost-effective
- 2 major foci:
  1. Instructions about pts' false beliefs
  2. Information about panic attacks (time-limited, not life threatening)

Treatment

Applied relaxation:

- Instil sense of control over anxiety & relaxation (eg: Herbert Benson's relaxation training)
- Standardized techniques for muscle relaxation and imagining of relaxing situations

Respiratory training:

- Control hyperventilation urge to control associated S_X (dizziness and faintness)

Treatment

In vivo exposure:

- Sequentially greater exposure of pt. to the feared stimulus to make the pt. desensitized to the experience

Psychosocial therapies:

- Family therapy: psychoeducation for support
- Insight oriented psychotherapy: helping pts. understand hypothesized unconscious meaning of anxiety, symbolism of avoided situation, need to repress impulses & secondary gains of symptoms

Summary

- One of the most common psychiatric disorders; lifetime prevalence 5%, more common in females
- Characterized by recurring panic attacks in the absence of triggers, with significant physical and psychological symptoms. As with other anxiety
- Comorbidities common

Summary

- Symptom-free periods b/w attacks with persistent concern about future attacks and maladaptive changes in behaviour to avoid attacks
- Often accompanied with agoraphobia
- Multifactorial etiology
- SSRIs & SNRIs and psychotherapy mainstay of treatment

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Thank You