CHAPTER 19.

FEAR AND ANXIETY

Introduction

"It remains unclear whether anxiety states are to be better conceptualized as several putatively distinct diagnostic entities or as one broadly conceived syndrome within which there are no clear boundaries between various manifestations of anxiety"

Vladan Starcevic (2006).

Arousal. Applied to the total organism, arousal refers to a state of readiness for activity, and involves increased sensory excitability, muscular tone and sympathetic and endocrine activity.

Anxiety is an unpleasant emotional state with qualities of apprehension, dread, distress and uneasiness, and is often accompanied by physical sensations such as palpitations, nausea, chest pain and shortness of breath.

Normal anxiety is applied to states of arousal/anxiety which occur in everyday life, in response to stimuli. It has an adaptive role and is a signal to take action. In normal anxiety the assessment of the danger is appropriate and the action taken is effective. The healthy person who has lost her/his pay-packet will be anxious about paying outstanding bills.

Fear is generally regarded to be an extreme form of normal anxiety. If an intruder comes into the house, most healthy persons will be fearful.

Pathological anxiety is diagnosed when there is inaccurate or excessive assessment of danger. The individual may be unable to make any response, or make an excessive protective response. The person with pathological anxiety may be so disabled that he/she is unable to conduct his/her usual duties, such as prepare a meal, or overestimate a danger and make a maladaptive adjustments (the person who is unduly anxious about lifts will have to take the stairs).

Normal anxiety vs. pathological anxiety. One perspective is that normal anxiety is a normal response to an abnormal situation (anxiety at being threatened by a mugger) and pathological anxiety is an abnormal response to a normal situation (anxiety at needing to leave the home).

Stress refers to external stimuli to which there is a need to adapt. In a stressful situation there may be a number of separate **stressors**. Stress is also used as a term to describe the state of being when subjected to stress (under stress; feeling stressed). It is not clear whether there is a difference between "feeling stressed" and "feeling anxious".

Yerkes-Dodson law (1908) has face validity in everyday life. This "law" describes a relationship between arousal and performance. As arousal increases so performance increases/improves, to a certain point, beyond which, as arousal continues to increase, performance declines. Sports coaches say that when the spots-person does not feel some pre-games tension they do not perform at their best. Some have even advised that when pre-game tension is no longer experienced, it is time to retire from top level competition. When performance anxiety (stage-fright) is excessive the pianist performs poorly (some take beta-blockers to reduce trembling hands).

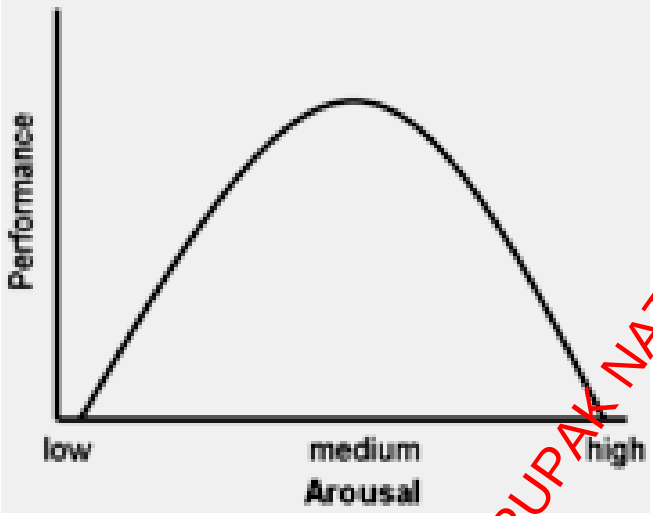


Illustration. The Yerkes-Dodson Law. As arousal increases, so does performance, to a certain point, beyond which increasing anxiety impairs performance.

DSM-IV Anxiety disorders

Two of the Anxiety disorders listed in the DSM-IV have been described here in separate chapters: Posttraumatic stress disorder is covered in Chapter 11, and Obsessive-compulsive disorder is covered in Chapter 13.

In this chapter the following will be considered:

- Generalized anxiety disorder
- Panic disorder without agoraphobia (commonly termed panic disorder)
- Panic disorder with agoraphobia (commonly termed agoraphobia)
- Social phobia
- Specific phobia

GENERALIZED ANXIETY DISORDER (GAD)

The diagnostic criteria of GAD are listed below. The first criterion is "Excessive anxiety about a number of events or activities". This wording suggests to some readers that it must be possible to identify the "events or activities" which trigger the anxiety, suggesting a similarity to phobic disorder. That is not the way to read this criterion. GAD symptoms have also been described as "unspecified or free-floating", and often, the patient cannot identify what "is making" them anxious.

GAD is common and can be greatly disabling. It has high rates of comorbidity, commonly occurring along with depression and other forms of anxiety. It is also associated with alcohol abuse, suicidality and high use of health care resources (Brown et al, 2001). Symptoms of GAD may lead to various primary care complaints including fatigue, sleep disturbance and chronic pain. GAD is a chronic condition which waxes and wains, and relapse is common.

DSM-IV Criteria for GAD

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school activities).
B. The person finds it difficult to control the worry.
C. The anxiety and worry are associated with three (or more) of the following
    1. restlessness or feeling keyed up or on edge
    2. being easily fatigued
    3. difficulty concentrating or mind going blank
    4. irritability
    5. muscle tension
    6. sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep).
D. The anxiety, worry or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Epidemiology

The 12 month prevalence of GAD in a community sample was 3.8% (Blazer et al, 1991). The lifetime prevalence has been estimated as 5-7% (Kessler et al, 2005).

GAD is twice as common in females.

Comorbidity

Over 2/3 (68%) of individuals with GAD have an additional Axis I diagnosis – most commonly, other anxiety disorders and depression. One study found personality disorder in 49% of people with GAD (Sanderson et al, 1994). It is associated with substance abuse and suicidality (Brown et al, 2001).

Theoretical aetiological models

Models of GAD have been advanced by various schools of thought. No single model is appropriate in every case, and probably all models have something to contribute to every case.

Biological models postulate people are predisposed to develop anxiety disorders by genetic inheritance.

Behavioural models are based on the learning theory. The behavioural models are often criticized as simplistic (Starcevic, 2005). Nevertheless, the therapy based on these models (behaviour therapy) has much to offer.

Cognitive models of anxiety disorders emphasize the role of specific beliefs and modes of thinking in influencing the experience of emotion.

The psychodynamic models invoke several concepts that are now often considered untenable (Starcevic, 2005). They propose anxiety occurs as a result of intrapsychic conflicts between sexual or aggressive urges and defences against these urges.

Genetic factors

Genetic factors appear to play a modest role in the aetiology of GAD. It is five times more common in the first-degree relatives of index cases than among the first-degree relatives of controls (Noyes et al, 1987). One study of twins concluded that GAD was moderately heritable (Mackintosh et al, 2006). There is a shared heritability for GAD and mood disorders (Kendler et al, 1992a), and recent the genetic risk for "internalizing psychiatric disorder" (mood and anxiety disorders) was estimated as 50% (Kendler et al, 2011). No specific loci have been identified.

Neurobiological mechanisms and neuroimaging

A wide variety of structures are believed to be involved in GAD.

The **locus coeruleus** and the sympathetic nervous system (SNS) are involved in fear and arousal, but their role in anxiety is yet to be fully elucidated.

The **hypothalamic-pituitary-adrenal** (HPA) axis, and the release of cortisol are involved in response to stress. Some evidence indicates that repeated exposure to stress my lead to deregulation of cortisol release and persistent anxiety.

The **amygdala** plays a central role in the mediation of fear reactions (LeDoux, 1998). The amygdala detects potential threats activates the SNS and HPA axis; through connections with the central midbrain, it mediates behavioural defence responses such as fight-or-flight and "freezing". However, the role of the amygdala may be less important in anxiety.

The amygdala can be separated into basolateral (BLA) and centromedial (CMA) subregions. Sensory information across multiple modalities enters the amygdala through the BLA, this leads to activation of CMA and a species specific defensive response (the reaction of a frightened cat is different to that of a pig). That is, the BLA is connected with primary and higher-order sensory and medial prefrontal cortices, and the CMA is connected with the mid-brain, thalamus and cerebellum.

In GAD, this pattern of connections is less distinct (Etkin et al, 2009). Other amygdala connection variations have been observed, including increased connectivity to the prefrontal cortex and the parietal lobe, and decreased connection with the insula

and cingulate. Further, in GAD, the CMA may have increased volume (Etkin et al, 2009).

Others have demonstrated abnormalities in the connection of the amygdala and the dorsal and ventral medial prefrontal cortex (Kim et al, 2010).

Psychosocial mechanisms

Clinical experience indicates that stressful life events may trigger GAD. The greater the number of negative life events experienced, the greater the likelihood of GAD (Blazer et al, 1987).

Early life experiences are important. A healthy parent-child relationship leads to the child developing a sense of control over the environment and a repertoire of adaptive responses. In the absence of such a relationship and development, the child may be vulnerable to anxiety (Chorpita & Barlow, 1998).

Prognosis

GAD is a chronic disorder. In one large study (Yonkers et al, 1996), the mean age of onset was 21 years and the average duration was 20 years. Although 80% received treatment, only 15% remitted after one year, and 27% had remitted after 3 years.

Remission rates are even lower in the presence of comorbid psychiatric disorders.

Treatment

Self-help books and activities may have a place (Hirai & Clum, 2006).

Psychological treatments take many forms, from a behavioural approach at one end of the spectrum, to psychodynamic psychotherapy at the other. Most therapists would claim to use some form of cognitive behaviour therapy (CBT). The original feature of cognitive therapy was the challenging of illogical and self-defeating thinking. However, the term CBT has absorbed a number of earlier stand alone treatments such as relaxation therapy, hypnosis, patient education, and even systematic desensitization (once the cornerstone of behaviour therapy), and it has emerged into an eclectic, and effective, active treatment.

Pharmacological treatments are helpful in the majority of cases. Alcohol is the most widely used substance in the management of anxiety. However, long-term use worsens anxiety and precipitates depression, in addition to serious physical consequences, and is discouraged. Antianxiety drugs are described in a separate chapter. Until recent years the term antianxiety drugs was synonymous with benzodiazepines. However, for various reasons (some substantiated and others not) various antidepressants (escitalopram, fluoxetine, paroxetine, sertraline and venlafaxine) are now regarded to be the first line pharmacological agents for the treatment of anxiety (Canadian et al, 2006).

PANIC ATTACK

The term panic comes from the Greek god, Pan. He was the god of flocks, music, sensuality and sexuality. He was also the god of nightmares, and took pleasure in frightening (panicking) people and animals in the woods. Panic symptoms were first described by Hippocrates circa 400 BC, and panic is known in all cultures. Modern accounts were recorded in the 19th century. Charles Darwin suffered panic disorder (Noyes & Barloon, 1997), but it was not until the 1960's that the high prevalence and disability which may accompany the disorder began to be fully recognized.

Illustration. Pan was a Greek god who enjoyed frightening (panicking) people and animals. He was (perhaps is) part man and part goat (ears, legs and horns).

The features of panic attack include:

1. palpitations
2. sweating
3. trembling or shaking
4. shortness of breath or sensation of smothering
5. feeling of choking
6. chest pain or discomfort
7. nausea or abdominal distress
8. feeling dizzy, unsteady, light-headed, 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. paresthesia (numbness or tingling sensations)
13. chills or hot flushes

AGORAPHOBIA

Agoraphobia is anxiety about, or avoidance of, places from which escape might be difficult (or embarrassing), or places where help may not be available. (It derives from the Greek, “agora”, meaning market place - the place where agricultural products are sold).

The features of agoraphobia include:

A. Anxiety about being in places or situations from which escape might be difficult (or embarrassing) or in which help may not be available. Agoraphobic fears typically involve characteristic situations including, being outside the home alone; being in a crowd or standing in a line; being on a bridge; and travelling in a bus, train, or automobile.
B. Situations are avoided (e.g., travel is restricted) or else are endured 1) with marked distress, 2) with anxiety about having a Panic Attack, or 3) with the presence of a supportive companion.

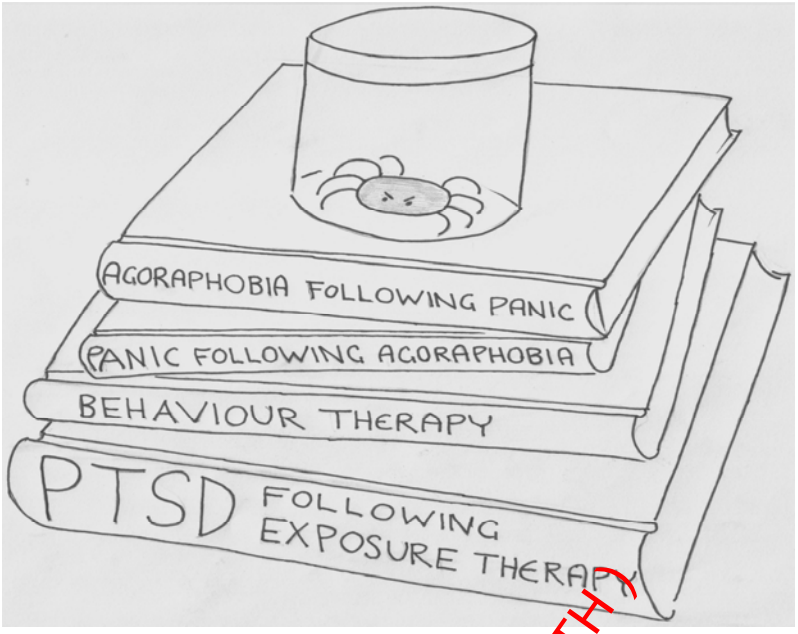
PANIC ATTACK +/- AGORAPHOBIA

The view held in the USA (reflected in the DSM-IV) is that panic attack is a core component of all anxiety disorders (with the exception of generalized anxiety disorder). Panic attacks are extremely frightening and it is thought that agoraphobia, for example, develops because of concern about experiencing a panic attack in a situation in which assistance will be difficult or embarrassing to obtain. Accordingly, what was once called panic disorder is now termed (in DSM-IV) **Panic disorder without agoraphobia**, and what was called agoraphobia is now termed (in DSM-IV) **Panic disorder with agoraphobia**.

The European view is otherwise (reflected in the ICD-10). Here, agoraphobia is conceptualized as being dominant over panic attack.

However, the evidence suggests a two-way causal relationship (Bienvenu et al, 2006).

The conceptualization has treatment implications. Where panic attack is considered primary, treatment often involves education and breathing exercises. Where the phobic component is considered primary, treatment often involves some form of exposure therapy. However, both approaches can be applied simultaneously.



PANIC DISORDER AND AGORAPHOBIA

Not surprisingly, panic disorder with agoraphobia includes panic attacks (described above) and agoraphobia (also described above).

Prevalence. Panic attacks occur in 7-9% of the population. A recent study found the lifetime prevalence of panic disorder to be 4.7% (Kessler et al, 2005). **Females** are twice as commonly affected. There are **two onset peaks**, one in early adult life (14-24 yrs) and one in middle age (45-54 yrs). Onset after 65 yrs is rare.

Genetics

There is a genetic predisposition to panic attacks and agoraphobia. For panic disorder the concordance rates in monozygotic is 2-3 times higher than in dizygotic twins. In a population based twin study the estimated heritability component of panic disorder was 30-40% (Kendler et al, 2001). Evidence suggests a 50% genetic and 50% environmental influence, polygenetic inheritance and heterogeneity across families (Schumacher et al, 2011).

Cannabis

Research (Zvolensky et al, 2006) suggests a lifetime history of cannabis addiction is significantly associated with an increased risk of panic attacks. It was found that those with a lifetime history of both panic attacks and cannabis use has a significantly lower age of onset of panic (19 years) than those with a lifetime history of panic attack and no cannabis abuse (28 years). The causal direction is unknown. It may be that those who are predisposed to develop panic treat themselves with cannabis; on the other hand, it may be that cannabis abuse triggers panic attacks.

Neurotransmitters

Evidence supports a role in aetiology of the **noradrenalin** pathways and the **locus ceruleus** (LC) in panic disorder. Most effective antianxiety drugs decrease LC firing.

A role for **serotonin** pathways in panic disorder is suggested by the observation that SSRIs have beneficial effects, and a role for gamma-aminobutyric acid (**GABA**) pathways is suggested by the beneficial effects of the benzodiazepines.

Prognosis

The disorder tends to a chronic relapsing course. Recovery rates vary from 25-75% in 1-2 year follow-up studies. In pharmacological trials, 50-70% of patients have an excellent acute response. In behavioural therapy programs, some trials have indicated improvement in 75% of patients at up to 9 years follow-up. While not symptom free, after some form of treatment, the majority make a functional recovery.

Treatment

Self-help books and activities have a place (Hirai & Clum, 2006). The following books are recommended (by Canadian et al, 2006):
Antony M, McCabe R. 10 simple solutions to panic: how to overcome panic attacks, calm physical symptoms, and reclaim your life. Oakland (CA): New Harbinger Publications: 2004
Barlow D, Craske M. Mastery of your anxiety and panic (MAP3). 3rd ed. (client workbooks for anxiety, panic, and agoraphobia). New York (NY): Oxford University Press: 2000.

As a lifetime history of cannabis dependence is significantly associated with a life time risk of panic attacks, suggesting that cannabis use may be an aetiological factor, the cessation of cannabis use is a sensible early step.

Non-pharmacological therapist involved treatments include exposure therapy, psychodynamic psychotherapy and cognitive-behaviour therapy (CBT). Exposure therapy includes gradual exposure (systematic desensitization) and rapid exposure (flooding). In large studies of exposure therapy, about 75% of patients have become symptom free, and this status has remained for years. Unfortunately, this therapy is anxiety-provoking and 25% of patients may drop out. Psychodynamic psychotherapy remains popular, but little research has been conducted on efficacy in panic disorder and agoraphobia. CBT is based on the theory that patients with panic disorder misinterpret their symptoms, and therapy focuses on challenging these misinterpretations.

The **pharmacological** treatment of anxiety disorders is covered in a separate chapter. The benzodiazepines are effective but have been relegated to second line status. The SSRIs and the selective noradrenalin and serotonin reuptake inhibitor, venlafaxine, are effective, lack the potential for addiction and are generally considered the medications of first choice.

Evidence suggests that pharmacological and non-pharmacological therapies have roughly equal efficacy. The advantage of non-pharmacological therapies (particularly CBT) is that they appear to have a lower rate of relapse at follow-up. The advantage of pharmacological therapy is a more rapid onset of relief. Some patients find either pharmacological or non-pharmacological treatment unacceptable, but the other acceptable. Each form has clinician and patient supporters. Combined treatment is an option (Furukawa et al, 2006).

SOCIAL PHOBIA (Social anxiety disorder)

There are many phobias (morbid fear or dread). From the clinical perspective a phobia is characterized by a fear which is persistent and intense, there is a compelling desire to flee or avoid the phobic place/object, and the fear is irrational. Agoraphobia (anxiety triggered by the thought of, or being in particular environments) has been described above.

In the DSM there are two other categories of phobia, specific and social phobia. While social phobia can be conceptualized as a specific phobia concerning social situations, it appears to have some features which justify separate categorization.

Social phobia is the experience of intense fear of being negatively evaluated by others or of being publicly embarrassed because of impulsive acts.

DSM criteria of social phobia

A. A marked of persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The individual fears that he or she will act in a way (or show anxiety symptoms) that will be humiliating or embarrassing.
B. Exposure to the feared social situation almost always provokes anxiety, which may take the form of a situationally bound or situationally predisposed Panic Attack.
C. The person recognizes that the fear is excessive or unreasonable.
D. The feared social or performance situations are avoided or else are endured with intense anxiety or distress
E. The avoidance, anxious anticipation, or distress in the feared social or performance situation interferes significantly with the person's normal routine, occupational (or academic) functioning, or social activities or relationships, or there is marked distress about having the phobia.

Social phobia has the highest **prevalence** of the phobias (and is the third most common psychiatric disorder, following depression and alcohol abuse). One study gives a lifetime prevalence of 8-12% (Shields, 2004). Social phobia is more common in **females** (as with other anxiety disorders). **Age of onset** is early, with two peaks, at 0-5 years and 11-15 years.

Resulting **disability** may be very high. People with social phobia frequently remain single and discontinue their education prematurely more often than people without this disorder (Schneier et al, 1994).

Comorbidity with other psychiatric disorders is very high (Liebowitz et al, 2005), and increases disability.

Genetic factors account for 1/3 of the variance in transmission. A major twin study found the concordance was greater for monozygotic (24.4%) than for dizygotic (15.3%) twins (Kendler et al, 1992b). Environmental factors are also important.

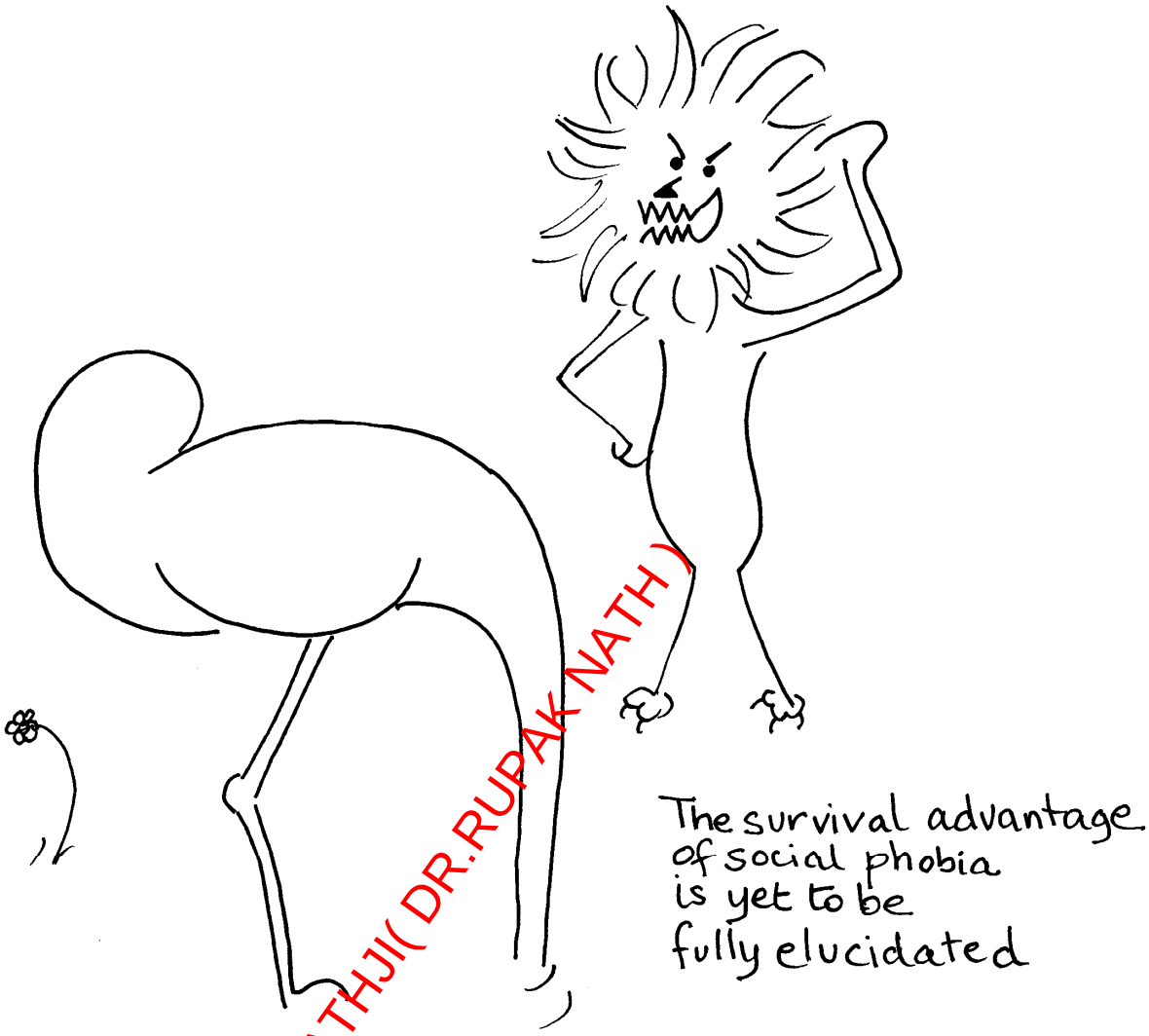
Neuroimaging: a meta-analysis of functional imaging (Etkin & Wagner 2007) in social anxiety disorder, specific phobia and PTSD in anxiety found that in all three disorders, hyperactivity was identified in the amygdala and insula.

Recent work has found, in social anxiety disorder, decreased gray matter volumes and decrease of structural connectivity between regions (Liao et al, 2011).

The **course** is chronic and unlikely to remit without treatment.

Treatment with antianxiety medication and CBT which involves a component of exposure may be beneficial. Pharmacological treatment gives more rapid relief, CBT treated patients are at less risk of relapse.

Demarcation between shyness and social phobia may be difficult. Non-generalized social phobia, is a term applied when symptoms are limited to specific situations such as public speaking. Interestingly, most individuals believe they are more nervous than others (Stein et al, 1994). There is a risk of medicalizing the human condition. Diagnosis should be limited to situations where individuals experience “significant distress and functional impairment”.



[On seeing this cartoon, Prof Dan J Stein made contact and drew attention to his important paper on the topic (Stein & Bouwer, 1997).]

SPECIFIC PHOBIA

The specific phobias feature marked and persistent fears which are excessive to any risks. Commonly feared objects include animals, insects, heights, injections/blood, and dental procedures, etc.

DSM criteria of specific phobia

A. Marked and persistent fear that is excessive or unreasonable, cued by the presence or anticipated presence of a specific object or situation (e.g., flying, heights, animals, injections, blood)
B. Exposure to the phobic stimulus almost always provokes an immediate anxiety response, which may take the form of a Panic Attack.
C. The person recognizes that the fear is excessive or unreasonable.
D. The phobic situation is avoided or else endured with intense anxiety or distress
E. The avoidance, anxious anticipation, or distress in the feared situation interferes significantly with the person's normal routine, occupational (or

academic) functioning, or social activities or relationships, or there is marked distress about having the phobia.

Many individuals with simple phobias are able to live a relatively normal life, making minor adjustments to avoid the feared object.

Sub-classification

1. animal type
2. natural environment type
3. situational type
4. blood/injection type (see next entry)
5. other type

Comorbidity with other psychiatric disorders is very high (>80%; Mannuzza et al, 1990). Specific phobias tend to co-occur with other specific phobias.

Lifetime prevalence is >10% (Kessler et al, 2005). Most common are the situational/environmental phobias, followed by animals and injection/blood phobias.

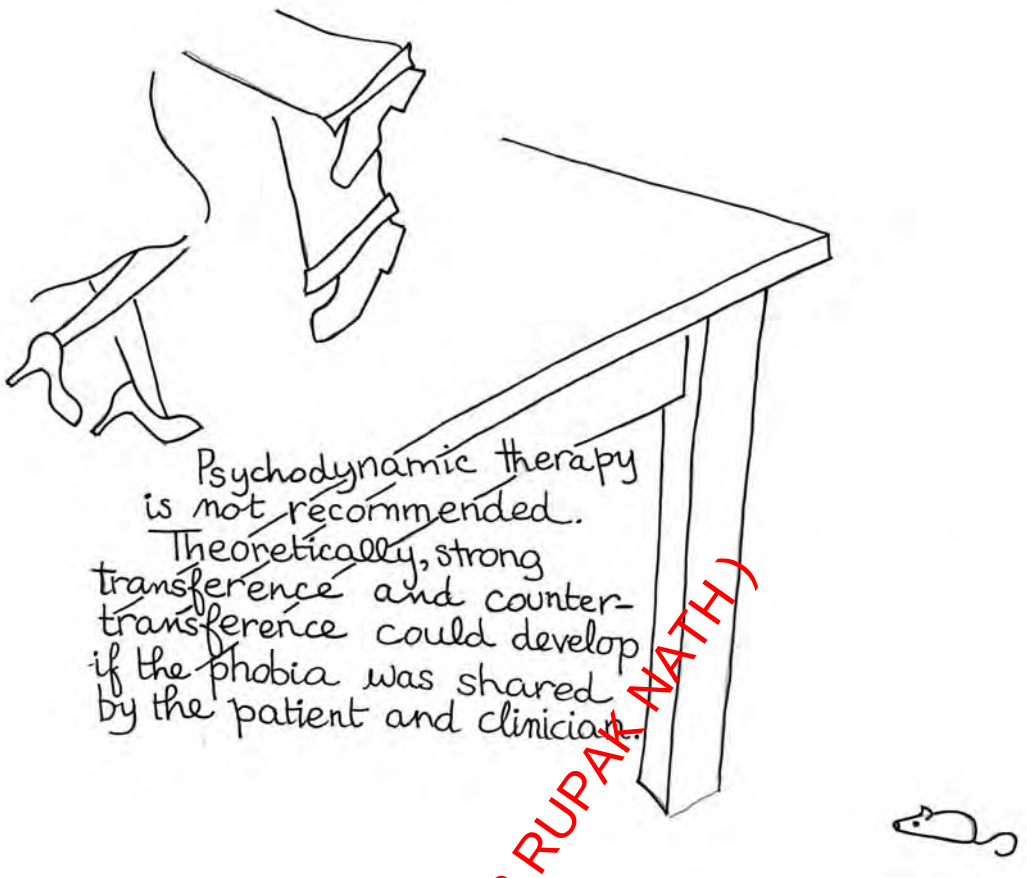
Age of onset appears to vary with the nature of the phobia. Animal phobia has the earliest age of onset +/- 7 years of age.

Genetic contributions are detectable, but also vary with the nature of the phobia.

Experiential/learning factors are also important.

Neuroimaging: see Neuroimaging under social phobia (above).

Treatment. Specific phobias are the most treatable of the anxiety disorders. CBT with an exposure component is recommended. The latter may be imaginal or *in vivo*. The latter may be difficult to arrange, in which case imaginal exposure is an effective alternative. Relaxation during exposure is an important component. Benzodiazepines have been used to reduce anxiety to enable patient co-operation with exposure.



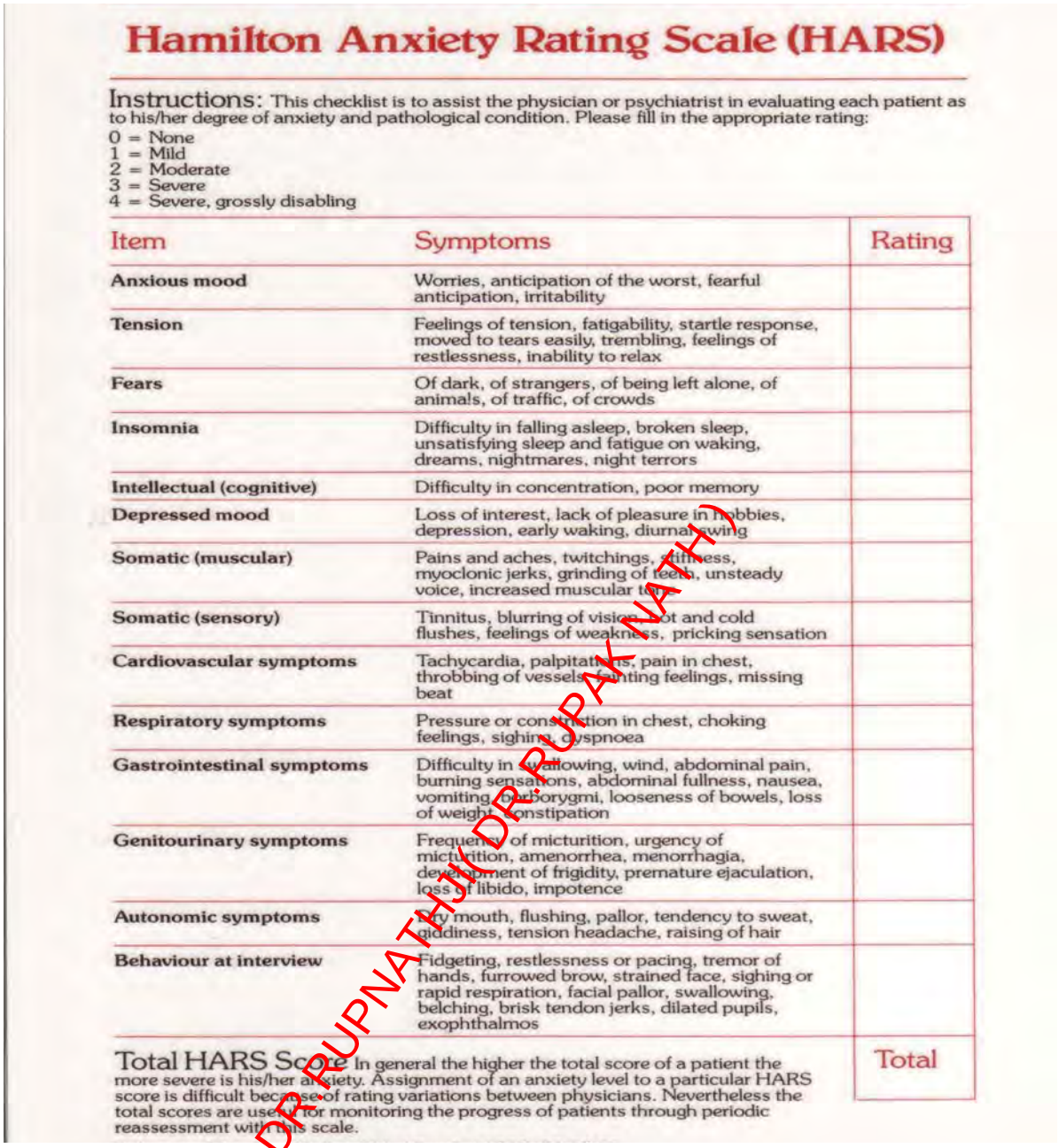
BLOOD/INJECTION PHOBIA

Blood/injection phobia appears to be a special case. In all other phobias, exposure is associated with increased sympathetic activity, with elevated BP and pulse. In blood/injection phobia, following brief sympathetic activity, parasympathetic activity predominates, leading to vasovagal syncope. This is most puzzling.

Accordingly, rather than maximal relaxation during exposure, patients are instructed to tense different muscle groups, thereby counteracting parasympathetic overactivity (Ost et al, 1991).

HAMILTON RATING SCALE FOR ANXIETY (HAM-A)

The HAM-A (Hamilton, 1959) is the most widely utilized assessment scale for anxiety symptoms. It is intended for use with people who have already been diagnosed with anxiety (that is, it is not a diagnostic tool, but a means of quantifying the experience of the patient). It is heavily focused on somatic symptoms and places reliance on the subjective report of the patient. The strengths of the HAM-A are that it is brief and widely accepted. The weaknesses are the focus on somatic symptoms and reliance on patient report. A printable version is freely available at www.cnsforum.com.



Hamilton Anxiety Rating Scale (HARS)

Instructions: This checklist is to assist the physician or psychiatrist in evaluating each patient as to his/her degree of anxiety and pathological condition. Please fill in the appropriate rating:

0 = None
1 = Mild
2 = Moderate
3 = Severe
4 = Severe, grossly disabling

Item	Symptoms	Rating
Anxious mood	Worries, anticipation of the worst, fearful anticipation, irritability	
Tension	Feelings of tension, fatigability, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax	
Fears	Of dark, of strangers, of being left alone, of animals, of traffic, of crowds	
Insomnia	Difficulty in falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night terrors	
Intellectual (cognitive)	Difficulty in concentration, poor memory	
Depressed mood	Loss of interest, lack of pleasure in hobbies, depression, early waking, diurnal swing	
Somatic (muscular)	Pains and aches, twitchings, stiffness, myoclonic jerks, grinding of teeth, unsteady voice, increased muscular tone	
Somatic (sensory)	Tinnitus, blurring of vision, hot and cold flushes, feelings of weakness, pricking sensation	
Cardiovascular symptoms	Tachycardia, palpitations, pain in chest, throbbing of vessels, fainting feelings, missing beat	
Respiratory symptoms	Pressure or constriction in chest, choking feelings, sighing, dyspnoea	
Gastrointestinal symptoms	Difficulty in swallowing, wind, abdominal pain, burning sensations, abdominal fullness, nausea, vomiting, borborygmi, looseness of bowels, loss of weight, constipation	
Genitourinary symptoms	Frequency of micturition, urgency of micturition, amenorrhea, menorrhagia, development of frigidity, premature ejaculation, loss of libido, impotence	
Autonomic symptoms	Dry mouth, flushing, pallor, tendency to sweat, giddiness, tension headache, raising of hair	
Behaviour at interview	Fidgeting, restlessness or pacing, tremor of hands, furrowed brow, strained face, sighing or rapid respiration, facial pallor, swallowing, belching, brisk tendon jerks, dilated pupils, exophthalmos	
Total HARS Score	In general the higher the total score of a patient the more severe is his/her anxiety. Assignment of an anxiety level to a particular HARS score is difficult because of rating variations between physicians. Nevertheless the total scores are useful for monitoring the progress of patients through periodic reassessment with this scale.	Total

Illustration. The Hamilton Rating Scale for Anxiety (HAM-A).

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