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Review Article

ANXIETY DISORDERS: A REVIEW

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Abstract

Anxiety is accompanied by a characteristic set of behavioural and physiological responses including avoidance, vigilance and arousal, which evolved to protect the individual from danger. In its non-pathological form, anxiety can be divided into two categories: state anxiety, a measure of the immediate, or acute, level of anxiety; and trait anxiety, which reflects the long-term tendency of an individual to show an increased anxiety response. In its pathological form, anxiety can severely interfere with normal life, and has been classified into six disorders described in the Diagnostic and Statistical Manual of the American Psychiatric Association¹: generalized anxiety disorder, social phobia, simple phobia, panic disorder, post traumatic stress disorder (PTSD) and Obsessive-compulsive stress disorder (OCD). There are various neurotransmitters that are evolved in the neurobiology of anxiety disorders such as GABA, 5-HT, noradrenaline etc. There are various neural circuits involved in anxiety like amygdala, hippocampus, locus cereulus but main region involved is that amygdala.

Keywords: Anxiety, GABA, 5-HT, GAD, OCD

The word anxiety is derived from the latin word "anxietas" (to choke, throttle, trouble and upset) and encompasses behavioural affective and cognitive responses to the perception of danger (Trivedi and Gupta, 2010). **According to Gross (2004)**, Anxiety is accompanied by a characteristic set of behavioural and physiological responses including avoidance, vigilance and arousal, which evolved to protect the individual from danger. Lifetime prevalence rates of the major anxiety disorders range between approximately 3% (OCD) and 12% (SAD) and are approximately two times greater among women than among men (Wittchen et al., 1994; Bersalu et al., 1998). The anxiety disorders with the greatest evidence for the efficacy of pharmacotherapy are generalized anxiety disorder (GAD), panic disorder (PD), social anxiety disorder (SAD), and obsessive-

compulsive disorder, whereas pharmacotherapy evidence for post-traumatic stress disorder (PTSD) is more limited. The therapeutics of obsessive-compulsive disorder are discussed elsewhere in this issue, whereas the treatment of specific phobias has been excluded because of space considerations. The medication classes most commonly used for GAD, PD, SAD, and PTSD are selective serotonin reuptake inhibitors (SSRIs) and serotoninnorepinephrine reuptake inhibitors (SNRIs), whereas other pharmacotherapy approaches include benzodiazepines (BZDs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), anticonvulsants, and atypical antipsychotics (Hoffman and Mathew, 2008).

Symptoms of Anxiety disorders

The subjective experience of anxiety typically

components namely physical component and emotional component which affect the cognitive function of an individual (Cates et al., 1996; Charles and Shelton, 2004; Shri, 2010). Anxiety symptoms are common in the community, and anxiety disorders are common in primary and secondary medical care settings. The disorders typically persist for many years, and are associated with significant personal distress, reduced quality of life, increased morbidity and mortality, and a substantial economic burden (Garner et al., 2009)

Emotional symptoms

- Headache
- Nausea and vomiting
- Sweating
- Trembling
- Stomach pain
- Ulcers
- Diarrhoea
- Feeling shortness of breath
- Hot flashes or chills
- Increased blood pressure

Physical symptoms

- Nervousness
- Worry
- Fear
- Irritability
- Insecurity
- Isolation from others
- Self consciousness
- Desire to escape
- Feeling that one is going to die

These emotional and physical sensations impair the cognitive processes such as thinking, decision-making ability, learning, memory and concentration (Shri, 2010).

Classification of anxiety Disorders

The DSM-IV (American Psychiatric Association) includes the following major categories of Anxiety Disorders: Post traumatic stress Disorder(PTSD), Generalised Anxiety Disorder (GAD), Panic Disorder (PD), Obsessive-compulsive Disorder (OCD), Specific Phobia, Social phobia (Social anxiety Disorder) (Trivedi and Gupta, 2011).

Post Traumatic Stress Disorder

Post traumatic stress disorder (PTSD) is a chronic, disabling disorder that affects 8%–9% of the population at some point in their lifetime.

The disorder is associated with significant morbidity and functional impairment, affecting both patients and family members, and its costs are similar to those of other severe mental disorders. The pathophysiology of PTSD involves a complex interplay between trauma-related factors and the neurobiological and psychosocial influences that determine individual differences in resilience and vulnerability (Connor and Butterfield, 2003). Post-traumatic stress disorder (PTSD) is a debilitating anxiety disorder that may develop after an individual has experienced or witnessed a severe traumatic event. Apart from symptoms of hyperarousal, characteristic features of PTSD include avoidance and amnesic symptoms (American Psychiatric Association 1994). Furthermore, imaging studies in PTSD patients have demonstrated volume reductions in the hippocampus (Elzinga and Bremner, 2002) that appear correlated with illness severity and the degree of cognitive deficit (Bremner, 1999). PTSD is frequently comorbid with other psychiatric disorders, including other anxiety disorders (SAD, OCD, and panic disorder), MDD, personality disorders, and substance abuse disorders, which may further complicate diagnosis and management.

Generalised anxiety Disorder

Generalised anxiety disorder (GAD) is a chronic and impairing disorder, independent of its substantial comorbidity with other mental disorders. But, it shares some risk and clinical similarities with other emotional disorder (Andrews et al., 2010). 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). DSM-IV defined GAD is not a tribal disorder. Some reports also indicate GAD is reliable as depression.

DSM-IV criteria for generalised anxiety disorder

- 1.Excessive anxiety and worry.
- 2.The person finds it difficult to control the worry
- 3.The anxiety and worry are associated with three of following six symptoms

- a. Restlessness
- b. Being easily fatigued
- c. Difficulty in concentration
- d. Irritability
- e. Muscle tension
- f. Sleep disturbance

The anxiety or worry cause significant distress or impairment in social, occupational or other important areas of function. It has been suggested that GAD could be considered the basic anxiety disorder because worry as its defining feature reflects a basic process of anxiety.

Obsessive- Compulsive disorder (OCD)

The DSM-IV-TR criteria for obsessions include unwanted thoughts, impulses, or images that cause great anxiety. These thoughts are not simply excessive worries about real life problems. Persons with obsessions attempt to ignore, suppress, or neutralize these thoughts, which are recognized as the product of their minds. The DSM-IV-TR criteria for compulsions include repetitive behaviours or mental acts that those affected feel driven to perform. Compulsions are aimed at preventing or reducing distress or preventing a dreaded event, though the behavior is not realistically connected to the dreaded event and is clearly excessive. (Charles and Shelton, 2004).

Panic disorder

Panic disorder is characterised by recurrent unexpected panic attacks, which are discrete periods of intense fear or discomfort accompanied by specific somatic symptoms and associated with characteristic sequelae such as fear and worry (American Psychiatric Association, 2000). A discrete period of intense fear or discomfort, in which 4 or more of the following symptoms developed abruptly and reached a peak within 10 minutes: such as palpitations, pounding heart or accelerated heart rate, sweating, trembling or shaking, sensations of shortness of breath or smothering, chest pain or discomfort etc. PD is associated with significant disability, elevated rates of suicidal ideation and suicide attempts. CBT and pharmacotherapy should be considered as first-line options for the treatment of PD (The Canadian Journal of Psychiatry, 2006).

Social phobia

Social phobia is persistent fear of one or more social situation in which a person is exposed to

unfamiliar person or to a scrutiny by others. Exposure to feared social situations provokes marked anxiety (American Psychiatric Association, 2000). SAD can be generalized or nongeneralized, depending on the breadth of social and performance situations feared. Generalized SAD is anxiety precipitated by most social and performance situations, and nongeneralized SAD is limited to a restricted number of social or performance situations (for example, public speaking). CBT and pharmacotherapy should be considered as first-line options for the treatment of SAD. Escitalopram, fluvoxamine, paroxetine, sertraline and venlafaxine are first-line pharmacotherapeutic choices (The Canadian Journal of Psychiatry, 2006).

DSM criteria of social phobia

1. A marked or 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.
2. Exposure to the feared social situation almost always provokes anxiety, which may take the form of a situationally bound or situationally predisposed Panic Attack.
3. The person recognizes that the fear is excessive or unreasonable.
4. The feared social or performance situations are avoided or else are endured with intense anxiety or distress
5. 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

Specific phobia

Specific phobia is a marked and persistent fear of circumscribed objects or situations (phobic stimuli), such as animals, blood, heights, closed spaces or flying. The fear is excessive or unreasonable. Exposure to phobic stimuli provokes an immediate anxiety response (American Psychiatric Association, 2000).

DSM criteria of specific phobia

1. 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)

2.Exposure to the phobic stimulus almost always provokes an immediate anxiety response, which may take the form of a Panic Attack.

3.The person recognizes that the fear is excessive or unreasonable.

4.The phobic situation is avoided or else endured with intense anxiety or distress

5.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

Gamma Aminobutyric Acid (GABA)

GABA is the main inhibitory neurotransmitter in the CNS. There are 2 subtypes of GABA receptors GABAA and GABA-B. Benzodiazepines bind to the benzodiazepine receptor complex located on the postsynaptic neuron. Such binding augments the effect of GABA leading to the opening of chloride ion channels causing the influx of chloride ions into the cell resulting in neuronal membrane stabilisation (Ressler and Nemeroff, 2000). Neuroimaging studies have reported reductions in GABA levels and GABA-A –benzodiazepine receptor binding in patients with anxiety disorder (Ressler and Nemeroff, 2000; Feldman and Weidenfeld, 2004; Roy-Byrne, 2005). GABA-benzodiazepine receptor are widely distributed in the brain and spinal cord but particularly concentrated in portions of brain thought to be involved in anxiety including the PFC, amygdala and hippocampus (Ressler and Nemeroff, 2000).

Serotonin

The central and peripheral norepinephrine system, because of its role in the adaptive response to acute physiologic and psychologic stressors has been a natural focus of investigation concerning the Pathophysiology of anxiety disorders (Feldman and Weidenfeld, 2004). Serotonergic neurons are implicated in the alteration of appetite, energy, sleep, mood and cognitive function in anxiety (Lesch and Gutknecht, 2004). Its role in anxiety is supported by its modulating effect on the locus ceruleus and its projections to amygdale; anatomical

structure almost conclusively implicated in anxiety. Fear and stress activate serotonergic pathways (Ressler and Nemeroff, 2000). The 5-HT system is significant for its established role in the treatment of anxiety disorders (Feldman and Weidenfeld, 2004). Serotonergic pathways arising from the raphe nuclei in the brainstem innervate a wide range of structures thought to be involved in anxiety including the frontal cortex, amygdala, hypothalamus and hippocampus (Feldman and Weidenfeld, 2004; Mathew et al., 2006; Dunn et al., 2004). Cellular pathology that may contribute to development of anxiety disorders includes abnormal regulation of 5-HT release and or reuptake or abnormal responsiveness to 5-HT signalling (Millan, 2003). Activation of 5-HT1A receptor is also involved in the induction of adrenocortical trophic hormone and corticosteroid secretion in response to stress (Bremner et al., 1996).

Noradrenergic system

Studies revealed that stress and anxiety cause a marked increase in NA release in several rat brain regions including hypothalamus, the amygdala and LC (Tanaka et al., 2000). Recently local administration of anti-sense oligodeoxynucleotide (AS-ODN) which corresponds to alpha-2A mRNA was shown anxiolytic effect (Shishkina et al., 2002). The role of the various NA receptor subtypes in mediating NA action on fear- and anxiety-related behaviours is therefore not settled. The precise location of the receptor subtypes within the complex circuitry mediating fear and anxiety responses is probably critical. Majority of noradrenergic neurons are found in the locus ceruleus. Altered noradrenergic signaling is linked to anxiety disorders. Sustained stimulation of locus ceruleus result in manifestation of anxiety symptoms. Stress-induced release of NE facilitates a number of anxiety-like behavioral responses too including stress-induced reduction of open-arm exploration on the elevated plus-maze, stress-induced reduction of social interaction behavior. Norepinephrine transporter-deficient mice have increased circulating catecholamines and elevated heart rate and blood pressure. Blockers of adrenergic β receptors have also been utilized clinically for treatment of performance anxiety.

Hormones of the HPA axis

Hormones of the HPA axis, such as cortisol, or corticosterone (in rodents), ACTH and CRF are usually increased in a state of fear and anxiety. They also appear to modulate the response to threatening events.

a. Corticotrophin releasing factor

Some abnormalities in the hypothalamic pituitary adrenal axis and central corticotrophin releasing factor (CRF) neuronal functioning have been identified in several anxiety disorders. Patients with combat-related post traumatic stress disorder have a pattern of control over production of CRF (Bermner et al., 1996; Dunn et al., 2004; Arborelius et al., 1999). CRF is a 41 amino acid peptide, a neurotransmitter with in the CNS that appears to be anxiogenic, depressogenic and proinflammatory. GABA inhibits CRF release (Charney and Deutch, 1996; Ressler and Nemeroff, 2000). In a rat model, a full postsynaptic CRF agonist, CRF(1-41), increased arousal at low dosage and had an anxiogenic action at higher doses (Henrichs and Jappa, 2001). This suggests that progressively increasing levels of CRF in the brain may ensure the transition from the initial state of increased arousal to the anxious state of expectancy in stressful situations.

b. Corticotrophin- releasing hormone

CRH is important mediator of stress response, as reflected by stress induced release of CRH from the hypothalamus into the hypothalamo-pituitary portal circulation resulting in activation of HPA axis and the increased release of cortisol and DHEA.(Charney and Deutch, 1996; Mathew et al., 2008). Stimulation of CRH-2 receptor results in reduced anxiety related behaviour. Increased CSF levels of CRH have been linked to PTSD by several studies (Dioro et al., 1993). The CRF binding protein (CRF-BP) may play an important modulatory role in CRF action.128 Interesting data consistent with a modulatory action of CRF-BP have recently been obtained with transgenic and knockout models: transgenic males overexpressing CRF-BP tend to show less anxiety, whereas the behavior of CRF-BP deficient mice was consistent with increased anxiety.

c. Cortisol

Psychological stress has been shown to increase the synthesis and release of cortisol. Cortisol has many different functions including mobilisation

of energy stores, increased arousal, vigilance, focused attention and memory formation, inhibition of growth and reproductive system. Cortisol increases the effects of CRH an conditioned fear and facilitate the encoding of emotion-related memory (Mathew et al., 2008). Dysregulation in cortisol secretions and in hypothalamic pituitary axis, which modulate stress responses have been observed in anxiety disorders such as GAD and PTSD (Dioro et al., 1993).

The neurosteroids

The neurosteroids are a novel, interesting class of neuromodulators synthesized in the brain directly from cholesterol. They appear to act essentially via an allosteric modulation of the GABAA receptor, although other receptors may also be involved. Majewska suggested that neurosteroids could play an important role in mood regulation. Several studies have shown that positive allosteric modulators (which potentiate GABA action), such as progesterone and allopregnanolone, have anxiolytic effects in various animal models. Neurosteroid synthesis is regulated by a peripheral benzodiazepine receptor (PBR) located on the outer mitochondrial membrane, and part of the anxiolytic effects of benzodiazepine could in fact involve increased neurosteroid synthesis. Compounds with a selective affinity for the PBR, such as FGIN-1-27, have shown an anxiolytic action in rats. Neurosteroids are currently attracting a lot of interest because of their potential role as natural, endogenous anxiolytics (Steimer, 2002)

Other peptides, neurotransmitters, and hormones

Several peptides, such as cholecystokinin (CCK), neuropeptide Y (NPY), tachykinins (substance P, neurokinins A and B), and natriuretic peptides (atrial natriuretic peptide or C-type natriuretic peptide) may play important roles in fear- and anxiety-related behaviors (Griebel G, 1999). CCK may be particularly relevant for panic disorders (Van et al., 1996; Rehfeld JF, 2000) and may influence cognitive processes (Dauge and lina, 1998). Excitatory amino acids (EAA), such as glutamate, are also important. In rats, microinjections of EAA into the dorsolateral PAG induce a flight reaction. Part of the effects mediated by *N*-methyl-D-aspartate (NMDA)

receptors may involve nitric oxide (NO). Nitric oxide synthase (NOS) inhibitors injected in the dorsolateral PAG have been shown to have anxiolytic effects, and psychological stress (restraint) induced an increased expression of neuronal NOS in the same area and in other areas related to defense mechanisms, suggesting that NO may participate in these defensive responses (Oliveira et al., 2001). We have also shown that anticipatory anxiety can lead to a decreased secretion of luteinizing hormone (LH) and testosterone in young, healthy male subjects (Schulz et al., 1996).

Genetic and environmental factors

Individual differences in sensitivity to threat or stress, and particular coping or affective styles appear to be critical predisposing factors for anxiety-related disorders. Genetic and environmental factors have been implicated.

Genetic determinants

A genetic basis for anxiety-related behaviours is now clearly established, notably through several family, twin, and adoption studies. In mice, targeted gene mutations have shown that modifying the expression of particular genes can have a profound effect on anxiety-related behavioral phenotypes (Tarantino et al., 2000; Clement et al., 2002). The quantitative trait locus (QTL) method is based on a comparison between the allelic frequency of markers and quantitative behavioral traits (Wehner et al., 2001; Polmin et al., 2000). It has been used to assess gene effects on fear, emotionality, and anxiety-related behaviours in mice from various genetic backgrounds (Clement et al., 2002; Wehner et al., 1997). Differences in vasopressin, oxytocin, and CRF action at the level of the amygdala (Roozendaal et al., 1992; Weirsmas et al., 1995), dopaminergic and GABAergic neurotransmission, basal vasopressin mRNA expression in the hypothalamic PVN (Aubry et al., 1995), and 5-HTT levels in the frontal cortex and hippocampus have been reported (Charney et al., 1995).

Environmental influences

The role of environmental influences in the etiology of anxiety is also well established (Craig et al., 1995). Early adverse experience is a major developmental risk factor for psychopathology (Sanchez et al., 2001; Heim et al 1999; Heim et al; 2001). Females were found to be more sensitive than males to the positive influences of

early stimulation (Fernandez et al., 1991). There are many examples indicate that the developmental processes that determine individual sensitivity to stressors, or emotionality, and coping behaviours involve complex interactions between genetic and environmental factors, and that anxiety-related phenotypes cannot be predicted on the sole basis of a genetic predisposition or early adverse experience.

Stress and anxiety

The brain is the central organ of stress and adaptation to stress because it controls and determines what is threatening, as well as the behavioral and physiological responses to the stressor. The adult, as well as developing brain, possess a remarkable ability to adapt and change with stressful and other experiences. Structural changes neuronal replacement, dendritic remodeling, and synapse turnover are a feature of the adult brain's response to the environment. Stress causes an imbalance of neural circuitry subserving cognition, decision making, anxiety and mood that can increase or decrease expression of those behaviours and behavioral states. In the short term, such as for increased fearful vigilance and anxiety in a threatening environment, these changes may be adaptive; but, if the danger passes and the behavioral state persists along with the changes in neural circuitry, such maladaptation may need intervention with a combination of pharmacological and behavioral therapies, as is the case for chronic or mood anxiety disorders (McEwen et al., 2012). Stress hormone effects on the activity of the amygdala and that of brain regions interconnected with the amygdala might directly alter the consolidation and recall of emotional memories, one of the core features of chronic anxiety, including post-traumatic stress disorder (PTSD) (Quervain et al., 2009). Moreover, the unique features of stress-induced neuronal remodeling in the amygdala and associated brain regions could be of relevance to studies of humans with mood disorders and PTSD. First, although neurons in the basolateral complex of the amygdala (BLA) undergo dendritic growth, neurons in the hippocampus and prefrontal cortex show atrophy following chronic stress. Consistent with these results, human neuroimaging studies have revealed enhanced responsiveness of the amygdala and

diminished responsiveness of the prefrontal cortex in patients with PTSD. There is also evidence for reduced hippocampal volume and function in patients with PTSD (Gurvits et al., 1996; Bremner, 2002; Gilbertson et al., 2002). Overactivity of the amygdala has also been reported in people with major depressive illness, along with atrophy of the hippocampus and prefrontal cortex (Sheline, 2003; Liang et al., 1990).

Change in neuronal morphology by stress

The effects of acute and chronic stress result in neuronal remodelling of synapses and dendritic branching in the BLA and medial amygdala (meA) that are accompanied by increases in anxiety (Vyas et al., 2002, 2004, 2006) and enhancement of fear conditioning (Conrad et al., 1999; Sandi et al., 2003; Wood et al., 2008). A single 2 h episode of immobilization stress in rats led to a delayed increase in spine density on principal neurons of the BLA and this was accompanied by greater anxiety-like behaviour (Mitra et al., 2005). Strikingly, the impact of chronic stress was not restricted to spines — it also triggered robust dendritic growth in pyramidal and stellate neurons of the BLA (Cornad et al., 1999; Sandi et al., 2003; Wood et al., 2008). Importantly, only those forms of chronic stress that triggered dendritic growth in the BLA also led to greater anxiety-like behaviour (Vyas et al., 2002). These changes probably involve increased corticosterone levels as a recent study showed that chronic treatment with 10 daily doses of high physiological levels of corticosterone also leads to dendritic hypertrophy in the BLA and to enhanced anxiety (Mitra and Sapolsky, 2008). The impact of chronic stress on the amygdala is also striking in its temporal persistence.

Neuro-anatomical structures involved in anxiety

Neuro anatomy model of fear (the response to danger) and anxiety (the feeling of fear that is disproportionate to the actual threat) include some key brain areas.

Brain stem

It mainly includes locus ceruleus, serotonergic raphe nuclei, and nucleus paragigantocellularis. They regulate arousal, attention and performance. To a large extent, levels of arousal are controlled by the same brain stem nuclei that is important for anxiety. Moderate arousal

increases attention and improves performance. Heightened arousal plays an important role in anxiety, leading, to hypervigilance and insomnia (Steimer, 2002)

Locus Ceruleus (LC)

Immediate consequence of fear and anxiety is autonomic activation. The locus ceruleus located in brain stem is the cores, which organize anxiety feelings. The LC contains a large proportion of the noradrenaline (NA) cell bodies found in the brain. It is highly responsive to alerting/stressful stimuli. Novelty of stimuli by itself is not sufficient to activate LC/NA system, but a stimuli that signal danger, may activate the system (Redmond and Huang, 1979).

It has widespread projection to stress and fear related neuroanatomical structures:

- Paraventricular nucleus (PVN) in the hypothalamus and activate the hypothalamo-pituitary-adrenocorticol (HPA) axis.
- Amygdale, mainly to central nucleus of amygdale (CeA)
- Prefrontal cortex (PFC)
- The bed nucleus of the stria terminalis (BNST)
- Hippocampus
- Periaqueductal gray (PAG)
- Hypothalamus
- Thalamus
- Nucleus tractus solitarius (NTS)

It is innervated by amygdale and other areas receiving visceral stimuli relayed by NTS (nucleus tractus solitaries).

Nucleus paragigantocellularis

Is the first one to receive afferent information from a variety of sources? It contains NA, serotonergic, cholinergic and excitatory amono acid receptor and involved in coordinating the activity of LC as well as other nuclei that control the sympathetic nervous system.

Limbic system

It involves amygdale, hippocampus, septal nuclei, and hypothalamus

Amygdale

It is well accepted that amygdale is involved in control of both fear and anxiety. It receives afferent signals from cortical and subcortical structures, including thalamus and parabrachial complex. Additional brain structures, including hippocampus and cortical pathways, provide more information on the situational context and relevant stimulus characteristics. It plays a

crucial role in the acquisition, retention, and expression of conditioned fear. Studies in rats also suggest that the basolateral nucleus of amygdale may play a crucial role in the consolidation of information that leads to the formation of a specific phobia. (File et al., 1998) BNST is considered to be part of extended amygdale. It appears to be the centre for the integration of information originating from the amygdale and the hippocampus and is clearly involved in the modulation of neuroendocrine stress response.

Prefrontal cortex

The frontal lobe integrate information from other parts of the brain and provide, as the executive part of the brain, the conscious experience of comprehending, planning, and decision making. It is the only cortical area with a direct connection to the limbic system. The right prefrontal cortex is more engaged in emotional responses than the left.

Conclusion

Anxiety disorders, though ubiquitous, are responsive to treatment. By using knowledge of the pathophysiology, an astute clinician can implement pharmacologic regimens with various mechanisms of action, leading to a positive outcome. Anxiety disorders that are untreated or undertreated can chronically expose the CNS to long-term increased glucocorticoid levels, which can lead to functional changes in the CNS.

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