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REVIEW ARTICLE

A Review on Generalized Anxiety Disorder

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ABSTRACT:

As in this century, people are more exposed to the competitive world which drastically reflects as the stressed out individuals that is mainly related to their nature of job, studies related and personal issues and so on. As a result considerable population was diagnosed with one or the other psychiatric disorders. This review is done to analyze the various underlying causes related to the neurotransmitters, family history leading to anxiety personality. And all these psychiatric problems are almost treatable under physician advice. The treatment includes pharmacological as well as patient counseling. Both should be carried out simultaneously in order to get beneficial outcomes. It is found that these patients try to keep themselves isolated in order to escape from the reality.

The prevalence of anxiety disorder is found both in children and adults. The incidence of GAD in men is half than in women. GAD is often associated with over fear and worrying. This patient mostly tries to avoid social interactions and spends time within a small circle. Based upon recent articles and literatures on detection, diagnosis and treatment of Generalized Anxiety Disorder this review has been written.

KEYWORDS: Neurotransmitters, Cognitive behavior, Mindfulness practice.

INTRODUCTION:

Anxiety disorders are now-a-days the most common psychiatric problem in prevalence.^[1,2] The incidence of GAD in men is half than in women. The GAD is usually associated with fear and over worrying and may also cause mild to severe effects to respiratory, cardiovascular, gastro intestinal or nervous system. It is equally found in both older and younger adults. Regarding children, the onset of anxiety disorders is early and develops gradually till adulthood. It also reflects in a negative way in academic, social, and family functioning. Anxiety disorders are sometimes caused as a result of disruptions in neuro endocrine, neurotransmitters and neuroanatomical.

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The genetic pre-disposition or bitter experiences tends to alter the brain structure or the function or the neurotransmitter signaling. Based on the culture, the prevalence of anxiety disorder in Asian is much lower when compared to Russian and US samples. The people with GAD often tries to avoid social interactions and spends time within a small circle. Gad has consequences and implications in different aspects of a person's life. About 1-5% general population report having GAD.^[3] GAD is generally characterized by excessive fear, avoids social interactions that is especially as a response to a particular object or situation and also in the absence of true danger.^[4,5,6]

DAIGNOSIS:

The significant problem in the present classification of anxiety disorders is the absence of known etiological factors and of specific treatments for different diagnostic categories.

The ABC model of anxiety widely helps in the diagnosis of the anxiety disorder and its management.^[7] The

simply called "ABC model of Anxiety" could be viewed as an interaction in space and time of alarms, beliefs and coping strategies.

 $[A] \Rightarrow$ alarms or emotional sensations or thoughts.

[B] => depends on the previous experiences, personal and cultural background.

[C] => specific behaviors or mental activity aimed at reducing anxiety.

In recent years it has been understood that the interplay between genetic, biological and stress factors that shape anxiety disorder, although it is not clear which is being inherited.

Neuronal circuits are governed by the multiple neurotransmitter systems. The most extensive are gamma amino butyric acid (GABA) and glutamate.

ANXIETY AND NEUROTRANSMITTERS:

Anxiety disorders are caused by neurotransmitters disruptions in some cases. In fact, the neurotransmitters govern the neuronal circuits.^[7] These are governed by the three major neurotransmitter systems namely the serotonin, dopamine and nor-epinephrine. The deficiency of one neurotransmitter is not responsible in causing the anxiety disorder; there is an interrelationship, multiple feedback mechanisms and complex receptor structure.

The involvement of the neurotransmitter and receptor systems in pathogenesis of anxiety disorders are as follows:

Serotonin:

The serotonergic pathways originate in the raphe nuclei and spreads widely throughout the forebrain. These are involved in maintaining anxiety, dopaminergic and noradrenergic pathways as well. The anxiety reduces in the increased level of the serotonergic tone, however the mechanism is not known.

GABA:

GABA is the main inhibitory neurotransmitter in the Central Nervous system [CNS]. Immediately anxiety is reduced by the modulation of GABA-ergic pathways. This pathway originates from the midbrain in the ventral tegmental area and substantia nigra, with projections to the cortex, striatum, limbic nuclei, and infundibulum.^[7]

Dopamine:

Dopaminergic pathways tend to affect the anxiety state in several ways. Its role is complex. Release of dopamine leads to acute stress in individuals.

Nor-Epinephrine:

It is a catecholamine. They are responsible in mediating the physiological symptoms of anxiety. The noradrenergic neurons originate in the pons and widely distributed in the CNS.

ANXIETY DEVELOPED BY ENVIRONMENTAL FACTORS:

The risk and vulnerability factors that potentially evolve from the environment in causing the anxiety disorders are discussed as follows,

The environmental factors that cause GAD has been classified into 5 major sections

- (1) Parenting and Family Environment.
- (2) Adverse life events.
- (3) Societal and cultural factors.
- (4) Gender Roles.
- (5) Genetic contribution.

(1) Parenting and Family Environment:

The role of parents influence in developing the anxiety. Parenting traits including the over control lack of warmth or rejection and over protection develop the anxiety disorders in child. ^[8] Father, parental influences siblings, culture are also involved in development of GAD.

(2) Adverse life events:

Psychotropic medications during pregnancy:

The anxiety and mood disorders in pregnant women are left untreated or they don't prescribe any psychotropic medications as they may expose the fetus to unfavorable conditions.^[9]

Pre and Perinatal:

Starting from the conception, the mother and fetus share the same environment. To explain this research has been conducted to explore the connections between pre and perinatal maternal stress and later child anxiety disorders including SAD (O' Keane and Scott 2005). They have introduced a new neurobiological model to explain it briefly. The anxious parent's child was also found to be anxious.

Life events:

The parental loss between 17 years and adult pathology in female had a relationship in development of GAD.^[10]

Post traumatic stress:

Individuals with horror experience and helplessness, faced serious injuries and fear of death are likely to develop generalized anxiety disorder.^[11]

(3) Societal and Cultural factors:

Every nation has its own religion, linguistic or cultural group. These groups are subject to same social and legal

structures instituted by country, but in most case these identities remain separate and intact.

(4) Gender Roles:

The females are more prone to anxiety disorder than males. The approximate ratio is 3:2. (Hidalgoet al 2001; Rapee and Spence 2004)

(5) Genetic Combination:

Both genetic and environmental contributions to vulnerability is there in case of anxiety disorder.^[12] They have more concentrated on the genes whose product regulates the HPA axis (Hypothalamus Pituitary Adrenal axis)^[13] and the monoaminergic signaling. In research the person with anxiety disorder is having both genetic and environmental influences. Genes are involved in acquisition, habituation and extinction of fears.^[13]

COGNITIVE BEHAVIOR THERAPY [CBT]: Shame and guilt in SAD (Social Anxiety Disorder):

Shame and guilt levels are elevated in case of patients having SAD. A study based on this showed that the SAD patients undergoing CBT for adult 2-3 weeks has shown a reduce in anxiety and this was correlated with the reduction of shame in those patients.^[14]

CBT for adults:

The study indicate that the most common anxiety disorder with a 12 month prevalence rates of 18.1% and lifetime prevalence rates of 28.8% ^[15] The CBT positive results varied widely for different types of anxiety disorder.

SEPERATION ANXIETY DISORDER:

Separation anxiety disorder is characterized by "developmentally inappropriate and excessive anxiety regarding from being separated from home or from person whom the patient is attached" (American Psychiatric Association [APA] 2000). Person having this SAD are significantly distressed when they are away from home or away from that particular person. And in addition those persons always take steps to avoid that separation. Those behaviors include crying, always attached to parents and almost refuse the activities that brings separation (for example: camp, sleepovers)^[16]

TREATING GAD AT SCHOOL LEVELS:

The 5 year child can also be affected by SAD and it may prolong for years if untreated. These children mostly have fewer friends, avoid classroom activities and avoid social interaction. But here is that many remain untreated.^[16]

THERAPEUTIC COMPONENTS:

The school based treatment is mainly by SASS (Skills for Academic and Social Success) has been done. ^[16] It is a kind of CBT program for school kids and adolescents to treat GAD.

SASS treatment is generally carried out with about 3-6 students of small groups.

The group sessions covers the five components.

- (i) Psycho education
- (ii) Realistic thinking
- (iii) Social Skills training
- (iv) Exposure
- (v) Relapse prevention

MINDFULNESS BASED STRESS REACTIONS [MBSR]:

In this multiple forms of mindfulness practice includes formal and informal meditation, hatha yoga (kabat-zinn, 1990). The formal includes breathing exercise, body scan based attention, walking meditation and eating meditation.^[17]

PHARMACOLOGICAL THERAPY:

The anxiety disorders are generally treated with four classes of medications, which are being discussed as follows

(a) Selective Serotonin Reuptake Inhibitors [SSRIs]:

SSRIs are generally considered as the first line therapy for anxiety disorders.^[18] These target the brain signaling system that uses the serotonin and its receptors. At present fluoxetine, paroxetine and sertraline are used as SSRIs^[19].

(b) Selective Nor-epinephrine Reuptake Inhibitors:

SNRIs act by inhibiting the serotonin and norepinephrine transporters. These are also used as the first line therapy for anxiety disorders. At present , venlafaxine and duloxetine are SNRIs used to treat anxiety disorder.

(c) Benzodiazepines:

Benzodiazepines are not used as first line of therapy. They were widely used in the past to treat anxiety disorder, but now it is not used because of risks associated with the chronic use. Benzodiazepines are most effective in case of short term treatment of the anxiety disorders. The commonly used benzodiazepines include trizolam, lorazepam and diazepam. Benzodiazepines and Barbiturates medication don't bind directly to the GABA receptor, instead the barbiturates increase the duration of the chloride channels open state whereas, the benzodiazepines increase the frequency of opening. This helps in reducing anxiety.^[20] Furthermore the usage of these results in developing tolerance.

(d) Anti seizure medications:

Anti-epileptics agents are used to treat anxiety disorders. Initially they were used for stabilizing mood disorders. Anti- Convulsants also have the capability in altering the GABA transmission; hence these classes of drugs are also used in treatment of anxiety.

CONCLUSION:

From this review we are able to know that the GAD is being most prevalent now a day. It is developed based on the parenting, environmental factors and cultural norms. The treatment is generally psychotherapy or pharmacotherapy. The Cognitive Behavior Therapy [CBT] is kind of treatment given to GAD patients and it is found to be effective. The pharmacotherapy includes SSRIs, SNRIs, benzodiazepines, anti-siezure drugs. For the diagnostic purpose the ABC model is found to be helpful. In addition the neurotransmitters role in development of GAD is also been known.

REFERENCES:

- Patrick Martin. Clinical Research: The Epidemiology of anxiety disorders: a review – Dialogues in clinical neuroscience 2003; Vol.5 No: 3: 281-298.
- Eric J.Lenze, Julie Loebach Wetherell. State of the art: A lifespan view of anxiety disorders – Dialogues in clinical neuroscience: 2011; Vol.13 No: 4:381-399.
- Christopher Gale, Oliver Davidson. Clinical Review: Generalized anxiety disorder - BMJ 2007:334:579-81.
- Stefan G. Hofmann, Anu Asnaani, Devon E. Hinton. Cultural Aspects in Social Anxiety and Social Anxiety Disorder Depress Anxiety. 2010 December; 27 (12): 1117–1127.
- Kathleen Herzig-Anderson, Daniela Colognori, Jeremy K. Fox, Catherine E. Stewart and Carrie Masia Warner. School-Based Anxiety Treatments for Children and Adolescents - Child Adolesc Psychiatr Clin N Am. 2012 July; 21 (3): 655–668.
- Christian Otte. Clinical research: Cognitive behavioral therapy in anxiety disorders: current state of the evidence - Dialogues in Clinical Neuroscience -2011; Vol 13. No. 4: 413-421.
- Alexander Bystritsky, Sahib S. Khalsa, Michael E. Cameron, Jason Schiffman. Current diagnosis treatment of anxiety disorders – P & T Jan 2013; Vol.38 No: 1: 30-57.
- Jill T. Ehrenreich, Lauren C. Santucci, Courtney L. Weiner. Seperation anxiety disorder in youth: phenomenology, assessment and treatment - Psicol Conductual. 2008 January 1; 16 (3): 389– 412.
- Christina A Brook, Louis A Schmidt. Social Anxiety Disorder: A review of environmental risk factors – Neuropsychiatric disease and treatment 2008; 4 (1): 123-143.
- Katja Beesdo, Susanne Knappe, Dipl-Psycha and Daniel S. Pine. Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for DSM-V - Psychiatr Clin North Am. 2009 September; 32 (3): 483–524.
- Lisa M Shin , Israel Liberzon. The Neurocircuitry of Fear, Stress, and Anxiety Disorders – Neuropsychopharmacology REVIEWS (2010) 35, 169–191.
- JohnPiacentini, TamiRoblek. Recognizing and treating childhood anxiety disorder – West J Med May 2002;176:149-159
- Ashwani Arya, Gulshan Sindhwani. A review on neural circuits in anxiety disorders- Asian J Pharm Clin Res 2016; Vol 9, Suppl. 3: 26-31.
- 14. Erik Hedman, Peter Strom, Angela Stunkel, Ewa Mortberg. Shame and Guilt in Social Anxiety Disorder: Effects of Cognitive Behavior Therapy and Association with Social Anxiety and Depressive Symptoms – 2003 April; PLOS ONE Vol.8 Issue 4.

- Stefan G. Hofmann, Jasper A. J. Smits. Cognitive Behavioral Therapy for adult anxiety disorders: A meta- analysis of randomized placebo controlled trails - J Clin Psychiatry. 2008 April; 69 (4): 621–632.
- Julie L. Ryan, Carrie Masia Warner. Treating Adolescents with Social Anxiety Disorder in Schools - Child Adolesc Psychiatr Clin N Am . 2012 January ; 21(1): 105–ix.
- Philippe R. Goldin, James J. Gross . Effects of Mindfulness-Based Stress Reduction (MBSR) on Emotion Regulation in Social Anxiety Disorder - Emotion. 2010 February; 10 (1): 83–91.
- Joshua P. Smith, Carrie L. Randall. Anxiety and Alcohol Use Disorders Comorbidity and Treatment Considerations - Alcohol Research: Current review: 415-431.
- Joshua P. Smith, Sarah W. Book. Anxiety and Substance Use Disorders: A Review - Psychiatr Times. 2008 October; 25 (10): 19–23.
- Elizabeth I. Martin, Kerry J. Ressler, Elisabeth Binder Charles B. Nemeroff. The neurobiology of anxiety disorder: Brain imaging, genetics and Psychoneuroendocrinology – Psychiatr Clin North Am. 2009 September; 32 (3): 549–575.