Anxiety Disorder

by

Isabella Cambra

Overview

Anxiety disorder is a common mental health disorder that is becoming more and more prevalent in society. Women are affected at twice the rate as men and we are seeing more anxiety in children now than ever before. According to the *National Institute of Mental Health*, anxiety disorder affects about 40 million adults in the United States from ages eighteen to fifty-four. It is characterized by intense feelings of worry, fear, uneasiness, and overwhelming stress in the body and mind that interferes with everyday activities. As a result, many people with anxiety disorder turn to food or alcohol to ease the tension.

Anxiety is different for each person but it is often due to a combination of the stress in our lives, bacterial imbalances in our gut, and common deficiencies in nutrients like vitamin B6 and zinc that are essential in making our neurotransmitters. Depletion of these nutrients leads to low amounts of the neurotransmitter GABA. GABA is a neurotransmitter that sends chemical signals to the brain to provide feelings of mental clarity and relaxation. Many drugs that are used to combat conditions like anxiety disorder are targeting GABA receptors in order to increase their compatibility with the GABA. When GABA is taken as an amino acid, it can alleviate some of the symptoms of anxiety disorder right away by lowering cortisol levels and providing some relief. Pharma GABA is a natural form of GABA that can also be used as a supplement. It is produced using a bacteria called lactobacillus hilgardii. Lactobacillus hilgardii is fermented so that it overproduces the amino acid, GABA, to be purified and made into a dietary supplement. In Japan, it is used to make kimchi, a food rich in GABA and probiotics.

Anxiety can be due to low GABA but it can also result from a lack of serotonin. With low serotonin anxiety, common symptoms include a wider range of phobias, fears, mental

worries, ruminating thoughts, and lack of confidence. The majority of serotonin is contained in the gastrointestinal tract making it important for proper digestion and motility. Since serotonin is a precursor to melatonin, having good serotonin levels is also crucial for sleep. When tryptophan and 5 HTP are taken as an amino acid, they can have similar results as GABA and Pharma GABA for low GABA.

Many studies have shown that heightened startle reflexes show a correlation with anxiety. Since cells in the amygdala process auditory, pain, and visual input, damaging or stimulating the amygdala in laboratory animals have resulted in lower levels of fear in the presence of danger, revealing the role of the amygdala in anxiety and allowing researchers to measure anxiety by measuring startle reflexes. After receiving input from the lateral and basolateral amygdala, the central amygdala relays information to the gray area of the midbrain. The gray area then sends the information to the area responsible for the startle reflex, the pons, in which damage impairs learned fears. During a frightening situation, people with severe anxiety have a highly reactive amygdala while the prefrontal cortex shows below-average activity. Many attempts to decrease anxiety rely on methods that try to increase prefrontal cortex activity. Prolonged anxiety can also cause damage to the hippocampus. Stress increases cortisol levels and metabolic activity in the hippocampus damaging and killing neurons. Since the hippocampus is the most important area of the brain for storing memory, the damage caused by anxiety can severely impair memory over time.

Although anxiety has not been linked to a single gene, infant behaviors have shown a correlation with anxiety in their adult life, allowing anxiety to be predicted. Inhibited and withdrawn infants often grow up to be fearful and shy adults. This is due to a gene that controls

the serotonin transporter which is important for serotonin reuptake. This particular gene reduces the reuptake of serotonin often leading to increased anxiety and awareness of threatening stimuli affecting many aspects of life. Since anxiety plays such a huge role in attitude and behavior, many methods of coping with anxiety are available today including reappraisal, social support, exercise, distraction, and behavioral and drug treatments.

Behavioral Treatment

One behavioral treatment that has been proven to result in significant improvements in the symptoms of psychological disorders is internet based cognitive behavioral therapy. Internet based cognitive behavioral therapy has shown a fifty percent success rate in treating psychological disorders. *Beck Institute for Cognitive Behavior Therapy* states that cognitive behavioral therapy is a method of treatment that focuses on changing the negative behaviors and thoughts of the patient. It challenges patients to use their cognition in order to realize their dysfunctional approach to information processing and establish a realistic perception of themselves. It demonstrates how in public, many people with anxiety disorders are focused on how they appear to others and they interpret feedback in a negative way. This leads to them avoiding social situations or behaving in a very inhibited manner. They tend to agonize over a stressful situation instead of looking at the reality of it and figuring out the most efficient ways to deal with it. Dwelling on these negative thoughts leads to fear and anxiety where there doesn't have to be.

Cognitive behavioral therapy tries to point this out to patients through a task-based approach that varies between each patient. According to Mayo Clinic's article, *Cognitive behavioral therapy*, it typically lasts between five to twenty sessions that are structured upon the assessment of the patient from the previous session. During the first session the patient describes their symptoms, views, problems, and the goals they wish to accomplish with treatment. For example, some patients describe trouble sleeping, making friends, or concentrating on work. They also often report problems in relationships or dealing with children. The assessment made by the therapist based on this information provides the structure for the next sessions where the

patient will reflect on their goals and the progress they have made so far. It also helps the therapist to be able to shape the treatment to each individual. This approach differs from other forms of therapy because it is designed to discuss specific information rather than whatever comes to mind. The structured system also enables the therapists to use time most efficiently and reassure that vital information is not left out.

Another important aspect of cognitive behavioral therapy is the emphasis it places on the completion of homework outside of the sessions. The patients who end up completing most of the homework they are assigned typically show the greatest improvement in their symptoms. Homework assignments are usually self-help strategies aimed towards teaching patients how to deal with their problems and gain control over their symptoms. They typically involve keeping a diary in order to monitor their thoughts and behaviors, tracking their progress in order to develop a more reality-based interpretation of life, and completing coping exercises such as gradually confronting their fears until they are no longer seen as stressors. This helps patients to examine the evidence of their distorted thoughts and change their beliefs to become more positive and constructive towards their goals.

Cognitive behavioral therapy has shown major reductions in the symptoms of patients with psychological disorders, however, it is typically administered by a clinician. This presents a problem because of the limited number of clinicians available for the growing population of people with psychological disorders. Internet based cognitive behavioral therapy is constructed around the same basic principals as cognitive behavioral therapy except it lacks the various barriers including the costs of the treatment, the limited number of clinicians available, the stigma around attending therapy sessions, and the difficulty of attending office appointments for

some. With online cognitive behavioral therapy, the patients have immediate access to their treatment and it is typically completed in only four to ten sessions. Clinical trials have shown that internet based cognitive behavioral therapy can significantly reduce the symptoms of many psychological disorders and the benefits often last longer than drug treatments.

Empirical Research Article on Behavioral Treatment

A study conducted by the Clinician Research Unit for Anxiety and Depression aimed to determine whether internet based cognitive behavioral therapy administered by a technician is just as effective as cognitive behavioral therapy administered by a clinician. In the study, *Internet Treatment for Generalized Anxiety Disorder: A Randomized Controlled Trial Comparing Clinician vs. Technician Assistance,* volunteers were recruited through a website called *VirtualClinic* which provided information about the research treatment program and how to apply. Participants were required to complete screening questionnaires that determined the severity of each patient's anxiety. Applicants who did not meet certain criteria were excluded from the trial. Applicants who passed the screening phase were assigned to either the technician-assisted group, the clinician-assisted group, or the control group. Then they were given access to the Worry program which consisted of six online lessons that represented the principals used in cognitive behavioral therapy. Each session provided information about problem-solving techniques, skills to help manage comorbid symptoms, and access to previous participant experiences. It also assigned homework to be completed prior to each session. Participants were advised to complete the whole treatment in ten weeks. During the technician-assisted treatment, participants received weekly emails or phone calls from a technician who read from a script that specified each of the topics covered during the online sessions and the activities the participant was meant to engage in. The technician was supervised by a clinician but was not allowed to give clinical advice. During the clinician-assisted treatment, clinicians had the same script but were also permitted to answer questions and actively engage in each participant's recovery. Participants assigned to the control group received absolutely no

treatment for eleven weeks but eventually received the clinician-assisted treatment. The results showed no differences between the participants who received the technician-assisted treatment from those who received the clinician-assisted treatment. They both showed significant improvements compared to the control group which showed no improvement at all. However, a three-month follow-up showed sustained results in the technician-assisted group where the clinician-assisted group continued to show some improvement.

Due to the significant improvement in patients who receive internet based cognitive behavioral therapy, I wholeheartedly support this treatment. Although I think that face-to-face cognitive behavioral therapy is more beneficial in the long run since it is far more intimate and personal, the rates of people with psychological disorders are on the rise and there is a limited number of clinicians available to meet with each client face-to-face. Not only does internet based cognitive behavioral treatment provide the opportunity for more people to receive help, but it also provides a more cost-effective means of obtaining it for the people who need help but do not have the money. This study further persuades me to support internet based cognitive behavioral therapy due to the similar results that participants who received the technician-assisted treatment showed to the participants who received the clinician-assisted treatment. Before I discovered this study I probably would not have supported internet based cognitive behavioral therapy due to the impersonal nature of it. However, there are some changes I would make if this study were to be conducted again. For example, I do not believe that the sample size was quite large enough. In order to obtain more accurate results, I think they should have waited until more people applied to the research treatment program or spent more time promoting it. Furthermore, a lot of the participants did not complete the online questionnaires given each week. Since the participants

who showed the highest completion rates for each questionnaire showed the greatest overall improvement in the end, I think the results would have been slightly different if more people had finished them. Lastly, instead of delaying the clinician-assisted treatment that the control group eventually received, I think they should have provided an attention placebo control group which would receive a treatment with a similar duration and amount of attention given to the technician-assisted and clinician-assisted groups but without providing any legitimate methods meant to produce improvements or reduction of symptoms in the participants.

Drug Treatment

Many alternative forms of treatment used to reduce symptoms of anxiety include the use of drugs. The most common drugs used to treat anxiety disorders include benzodiazepines and selective serotonin reuptake inhibitors (SSRI's). SSRI's are typically used in the treatment of anxiety disorders and are often said to be less addictive. According to a study conducted by *Dialogues in Clinical Neuroscience*, all SSRIs have proven to be very effective in treatment. A common SSRI used to treat anxiety today is known as paroxetine. Paroxetine is a synthetic drug known to be the most potent SSRI available. It is typically taken in twenty milligram doses once a day for adults when prescribed for anxiety disorders, however, dosing may also vary between each individual. Children are generally not supposed to take paroxetine unless it is prescribed by their doctor. It usually comes as a water-soluble tablet meant to be swallowed whole but it can also be taken in liquid form and measured out with a teaspoon. Paroxetine should be taken orally and with food in the morning or evening and preferably at the same time every day. It is prescribed for an average of six to eight weeks but sometimes takes a month or longer until people start to experience the benefits.

According to *MedlinePlus Drug Information*, people taking paroxetine may experience a variety of different symptoms including headaches, dizziness, weakness, difficulty concentrating, vomiting, diarrhea, and nausea. Serious side effects can include fevers, chest pain, and difficulty breathing. If someone were to overdose on paroxetine they might experience hallucinations, seizures, or even fall into a coma. Although SSRIs are not meant to be addictive, discontinuing treatment abruptly after six weeks or missing several doses has often led to withdrawal

symptoms that include nausea, dizziness, flu-like symptoms, and general feelings of lethargy and uneasiness.

Paroxetine ultimately works to improve cognitive and emotional processing regulated by the hippocampus allowing people to lead normal lives and enjoy social activities. Since serotonin is the neurotransmitter largely associated with feelings of happiness and well-being, serotonin deficiencies often result in depression and anxiety. Because serotonin regulates hippocampal output, paroxetine primarily targets the hippocampal cells in order to normalize cognitive and emotional output under stressful conditions. According to the study *Changes in Cerebral Cortex and Limbic Brain Functions after Short-Term Paroxetine Treatment in Panic Disorder: An [18F]FDG-PET Pilot Study,* serotonin-specific reuptake inhibitors like paroxetine can also result in increased glucose metabolism rates in multiple areas of the limbic brain and cerebral cortex. Paroxetine works to reduce the symptoms of anxiety and other psychological disorders by increasing the amount of serotonin that reaches the brain. Once serotonin is released into the synaptic cleft by the presynaptic neuron, serotonin neurotransmitters that do not bind to postsynaptic receptors are left in the synaptic cleft. By binding to the 5-hydroxytryptamine receptors and inhibiting the reuptake of serotonin to the presynaptic neuron, paroxetine causes a greater amount of serotonin to remain in the synaptic cleft. The excess serotonin that remains in the synaptic cleft continues to stimulate the postsynaptic neuron and provoke a stronger response improving overall mood and relieving the symptoms of anxiety and depression.

However, *Selective Serotonin Reuptake Inhibitors (SSRIs)* states that prolonged usage of any SSRI can lead to neuromuscular abnormalities, altered mental status, dysfunction in the autonomic nervous system affecting digestion, heart rate, breathing, and blood pressure, and an

increased risk of bleeding. Moreover, many SSRIs including paroxetine can reduce sex drive and are highly expensive.

Empirical Research Article on Drug Treatment

The study, *Paroxetine efficacy in the treatment of generalized anxiety disorder,* aimed to determine the success rates of paroxetine in alleviating the symptoms of anxiety disorder compared to those of imipramine and 2-chloromethyl diazepam in order to find an alternative to benzodiazepines for treating the symptoms of anxiety. The study was conducted over a two-year period but lasted eight weeks for each participant. Eighty-one patients who fulfilled specific requirements were recruited to participate in the study. They had to be between the ages of eighteen and sixty-five and have a DSM-IV diagnosis of anxiety. They also had to pass a series of online tests and an interview in order to qualify. They were randomly assigned to either the paroxetine treatment, the imipramine treatment, or the 2-chloromethyl diazepam treatment and further assessments were made after two, four, and eight weeks of using the treatment. Side effects from the treatment varied among each group. The 2-chloromethyl diazepam group experienced the highest rates of drowsiness, the paroxetine group experienced the most nausea, and the imipramine group experienced the most anticholinergic side-effects. Significant improvement in the symptoms of all of the groups was observed after two weeks but results showed that the most significant improvements were seen in the 2-chloromethyl diazepam group. However, from week four until the end of the study, the paroxetine group and the imipramine group showed the most significant improvements. The 2-chloromethyl diazepam group showed the most overall improvement in somatic symptoms but the paroxetine group and the imipramine group showed the most improvement in psychic symptoms. By the end of the trial, data showed that both of the antidepressant treatments were superior to the 2-chloromethyl diazepam treatment since they showed the highest rates of overall improvement. Ultimately, the study

concluded that paroxetine is an effective form of treatment and is comparable to that of imipramine for treating the symptoms of anxiety.

Similar to the behavioral treatment study, if this study were to be conducted again I would change the sample size and diversity in order to better represent the population. Also, even though there were quite a few participants who dropped out, it still seemed somewhat equal between each group. Furthermore, I would have liked to know how the results of the paroxetine treatment, the imipramine treatment, and the 2-chloromethyl diazepam treatment would have compared to an attention placebo control group that received a placebo pill in place of a treatment or a cognitive behavioral therapy group to determine how cognitive therapy would compare to drug treatments. Overall I think this study was successful in determining the efficacy of paroxetine to treat the symptoms of anxiety. I also largely support the attempt to find an alternative to benzodiazepines to treat anxiety.

However, even though a significant improvement was observed in the group that received the paroxetine treatment, I will never support the use of prescription drugs unless cases are so severe that prescription drugs are required in order to sustain a healthy life. I believe that behavioral treatments are the most effective in the long run and are the only form of treatment that doesn't decrease longevity. Plus, there are typically no side effects to a behavioral treatment. My personal experience with autoimmune diseases has shown me how damaging prescription drugs can be especially if taken at an early age, and how beneficial simple lifestyle changes can be including altering diet. Doctors are prescribing more and more drugs than ever before that are ultimately causing more symptoms and diseases. According to the article *Psychiatric Polypharmacy Continues to Grow*, sixty percent of patients that visit the doctor end up receiving

a drug prescription and thirty-three percent of the time a drug is prescribed, it leads to the patient obtaining at least three more medications soon afterwards. If I were to conduct this study, I would add another group to determine how a drastic change in diet would compare to a drug treatment and a behavioral treatment in improving the symptoms of anxiety.

Works Cited:

Robinson, Emma, et al. "Internet Treatment for Generalized Anxiety Disorder: A Randomized Controlled Trial Comparing Clinician vs. Technician Assistance." *PLOS ONE*, Public Library of Science, 19 Oct. 1966, journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0010942.

Rocca, Fonzo P., et al. "Paroxetine Efficacy in the Treatment of Generalized Anxiety Disorder."*Wiley Online Library*, May 1997, www.bing.com/cr?IG=377127D9525E407DA65CBE9F1358D81C&CID=18944065D6FC655F137C4B5AD7FA6473&rd=1&h=nsoE6uz5BREGpyGH-Bt32bg0Kh_98_hD0rATOj9-pdQ&v=1&r=https%3a%2f%2fwww.researchgate.net%2fpublication%2f14021222_Paroxetine_efficacy_in_the_treatment_of_generalized_anxiety_disorder&p=DevEx,5092.1.

Dale, Elena, et al. "Effects of Serotonin in the Hippocampus: How SSRIs and Multimodal Antidepressants Might Regulate Pyramidal Cell Function." *CNS Spectrums*, Cambridge University Press, Apr. 2016, www.ncbi.nlm.nih.gov/pmc/articles/PMC4825106/.

Sim, Hyun-Bo, et al. "Changes in Cerebral Cortex and Limbic Brain Functions after Short-Term Paroxetine Treatment in Panic Disorder: An [18F]FDG-PET Pilot Study." *Psychiatry Investigation*, Korean Neuropsychiatric Association, Sept. 2010, www.ncbi.nlm.nih.gov/pmc/articles/PMC2947810/.

Cassano, Giovanni B. “Psychopharmacology of Anxiety Disorders.” *Dialogues in Clinical Neuroscience*, Les Laboratoires Servier, Sept. 2002, www.ncbi.nlm.nih.gov/pmc/articles/PMC3181684/.

“Cognitive Behavioral Therapy.” *Mayo Clinic*, Mayo Foundation for Medical Education and Research, 11 Aug. 2017, www.mayoclinic.org/tests-procedures/cognitive-behavioral-therapy/home/ovc-20186868.

Gever, John. “Psychiatric Polypharmacy Continues to Grow.” *Medpage Today*, MedpageToday, 4 Jan. 2010, www.medpagetoday.com/psychiatry/generalpsychiatry/17785.

Ogbru, PharmD Omudhome. “Paroxetine, Paxil, Pexeva: Drug Facts, Side Effects and Dosing.” *MedicineNet*, www.medicinenet.com/paroxetine/article.htm.

Buet, Sylvia. “HOW EFFECTIVE IS ONLINE CBT THERAPY?” *Success Rates: How Effective Is Online CBT Therapy?*, 10 June 2013, www.anapsys.co.uk/cbt-therapy.htm.

Ogbru, PharmD Omudhome. “Paroxetine, Paxil, Pexeva: Drug Facts, Side Effects and Dosing.” *MedicineNet*, www.medicinenet.com/paroxetine/article.htm.

Rivas, Anthony. “How Antidepressants Work In The Brain: A Comprehensive Guide.” *Medical Daily*, 3 June 2015, www.medicaldaily.com/how-antidepressants-work-brain-comprehensive-guide-336250.

“NAMI.” *NAMI: National Alliance on Mental Illness*, www.nami.org/Learn-More/Treatment/Mental-Health-Medications/Paroxetine-(Paxil).

Industries, Ltd. Wako Pure Chemical. “Researches for Depression Selective Serotonin Reuptake Inhibitors (SSRI).” *Wako Pure Chemical Industries, Ltd.*, www.wako-chem.co.jp/english/labchem/product/life/SSRI/index.htm.

“Paroxetine.” *MedlinePlus Drug Information*, medlineplus.gov/druginfo/meds/a69