

5-2022

Anxiety and Immunity: Affecting the Body and the Mind

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Honors Senior Thesis

B.S. Biology - May 2022

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Anxiety and Immunity: Affecting the Body and the Mind

TABLE OF CONTENTS

TABLE OF CONTENTS	1
ABSTRACT	3
INTRODUCTION	3
Anxiety Disorders	3
Immune System Disorders	10
Links Between Anxiety Disorders and Immune System Disorders	12
METHODOLOGY	13
RESULTS	14
DISCUSSION	16
Alopecia Areata	16
Fibromyalgia	17
Asthma	18
Hashimoto's Thyroiditis	19
Type I Diabetes	20
Conclusion	21
Future Research Directions	22
Limitations of this Study	23
SUPPLEMENTAL FIGURES	24
APPENDIX	33

Sample Survey	33
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WORKS CITED	35
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ABSTRACT

Speculations have been made within the scientific community that there is a link between the underlying mechanisms that impact anxiety disorders and immune system disorders. While many correlations between these disorders have been observed through various immune system disorder studies, this subject is still severely under-explored. In order to examine the potential relationship between anxiety disorders and immune system disorders, a survey was conducted and distributed among the student population at the University of Nebraska at Omaha. This survey collected data by asking a variety of questions that pertained to anxiety and immune system disorders diagnoses within the student population and their families. The survey results indicated that there is a high prevalence of anxiety disorders in individuals with immune system disorders. Additional research will need to be conducted before any conclusive links can be established. Future research may examine whether this link is only found in certain types of immune disorders, whether age and/or cultural influences have an impact on this relationship, assess 5-HT level correlations, and explore the role of gut inflammation in this link.

INTRODUCTION

Human body systems are greatly intertwined and no single system can function without the aid of another system; when one body system is impacted by complications such as diseases and disorders, other body systems are also affected due to the connections between them. The processes that occur within these human body systems are complex and may often be associated with related medical problems and disorders. External stressors, whether positive or negative, may also further have a significant impact on the normal function of the bodily system as stress has been shown to have some impact on all major body systems.² The effects that stress has on anxiety and on the immune system can be compared and contrasted to further research on the relationship between these disorders. When long bouts of stress occur, there is an increase in cortisol and corticotropin hormones within the body for longer periods of time, promoting the formation of clinical anxiety and mood disorders.¹⁵

ANXIETY DISORDERS

Anxiety disorders are one of the most prevalent types of disorders in the United States with about 1 in 4 individuals reporting a lifetime history of at least one anxiety disorder.¹ Simple, everyday items such as stressors, diet, exercise, certain medications, aging, etc may also impact the prevalence and severity of anxiety disorders.^{8,11,13} The symptoms associated with anxiety disorders may also be negatively influenced by some physical health conditions, such as thyroid problems or heart arrhythmia, and also the consumption of caffeine or other substances/medications.⁸ The exact definition of anxiety disorders can vary greatly between various sources as there are several subclasses of anxiety disorders. The five different major types of anxiety

disorders include Generalized Anxiety Disorder (GAD), Obsessive-Compulsive Disorder (OCD), Panic Disorder, Post-Traumatic Stress Disorder (PTSD), and Social Phobia (or Social Anxiety Disorder).⁴ Diagnoses for each of these disorder types are outlined in the Diagnostic and Statistical Manual of Mental Disorders Version 5 (DSM-5); this disorder diagnostic criteria can be found below with each disorder explanation.¹²

Some known general risk factors for anxiety disorders may include shyness or feeling distressed or nervous in new situations in childhood, exposure to stressful and negative life or environmental events, and a history of trauma (such as abuse, neglect, divorce, drug abuse, separation, etc).^{8,11,13} Biological sex also has an impact on the prevalence of anxiety diagnosis as women as more likely than men to experience and be diagnosed with anxiety disorders.^{7,9,13} Anxiety disorders have been shown to run in families, indicating that the underlying mechanisms that contribute to the development of an anxiety disorder are hereditary.^{8,9,13}

The most prevalent type of anxiety disorder is GAD. GAD is generally described as persistent and excessive worry about rather insignificant events for long periods of time.^{4,5,6,7,8,9,11} GAD affects 6.8 million adults or 3.1% of the U.S. population, yet only 43.2% are receiving treatment.⁹ GAD disorder diagnosis is present in 22% of patients who complain of anxiety problems.⁸ Women are twice as likely to be affected as men.^{7,9} All of these statistics indicate that GAD is the most commonly reported type of anxiety in the adult population.

When assessing for GAD, clinical professionals look to the criteria outlined in the DSM-5. Symptoms may vary slightly between patients but, in general, GAD symptoms can be outlined enough to provide a basic foundation for diagnostic criteria. These clinical professionals that are considering a GAD diagnosis are looking for the following:⁶

- The presence of excessive anxiety and worry about a variety of topics, events, or activities; this worry occurs more often than not for at least six months and is clearly excessive.
- Feelings of worry are very challenging to control; this worry in both adults and children may easily shift from one topic to another.
- The anxiety and worry are accompanied by at least three of the following physical or cognitive symptoms: edginess or restlessness, tiring easily or more fatigued than usual, impaired concentration or feeling as though the mind goes blank, irritability (which may or may not be observable to others), increased muscle aches or soreness, difficulty sleeping (due to trouble falling asleep or staying asleep, restlessness at night, or unsatisfying sleep). In children aged 18 years and younger, only one of these symptoms is necessary for a diagnosis of GAD.

In order to give a diagnosis of GAD, these symptoms also must be unrelated to any other medical conditions and cannot be explained by a different mental disorder or by the effect of substance use, including prescription medication, alcohol, or recreational drugs.^{1,6,8,9,13} GAD is mostly diagnosed along with other mental disorders, such as depressive and anxiety disorders,

but this is not a requirement for diagnosis.^{5,7,9,10,11,12} Individuals with GAD don't typically engage in compulsive and ritualistic behaviors to cope with their anxiety.¹⁶

Another common type of anxiety disorder is Obsessive-Compulsive Disorder (OCD). OCD affects an estimated 1.0% to 1.2% of the U.S. population.⁹ OCD prevalence in men and women varies depending on the study and data presented; some studies claim that OCD is equally common among men and women while other studies state that OCD is about twice as likely to occur in women.⁹ The average age of onset for OCD symptoms is 19, while 25% of OCD cases start exhibiting symptoms by the age of 14 years old.^{9, 16, 22} One-third of affected adults first experienced symptoms in childhood but these symptoms are typically not severe enough to justify a diagnosis this early in life.⁹

As part of the revision of the DSM from the fourth version to the fifth, the newest DSM version that was released in 2013 changed the OCD diagnosis from being included as part of a GAD diagnosis to the disorder being its own disorder in the “Obsessive-Compulsive and Related Disorders” category.^{15, 19, 22} This revision indicated that there is one major difference between GAD and OCD: the presence of compulsions and/ or obsessions.

Individuals with OCD tend to engage in compulsive and ritualistic behaviors as a form of coping mechanism for their anxiety by creating relief from the fear of what the consequences would be without engaging in these repetitive behaviors.¹⁶ These behaviors may be physical or mental actions and are often referred to as compulsions.^{4, 5, 15, 16, 22} In severe cases, these compulsions can take up more than an hour each day to complete and affect daily life.^{15, 16, 18, 22} One may fear that if these actions are not completed then something bad may happen.^{5, 15} Some examples of compulsions may include extremely frequent hand washing, counting, checking, cleaning, losing control of behavior, etc.^{4, 15, 16, 22}

OCD can also create repetitive thoughts or mental images similar to compulsions called obsessions.^{4, 5, 15, 16, 17, 22} These obsessions may be exhibited in the form of excessive fear of germs, unwanted or forbidden thoughts of sex or religion or harm, aggressive thoughts towards others, having things in symmetrical or perfect order, etc.

When considering whether a patient has OCD, a clinician will utilize the Y-BOCS scale; this scale is a survey that the clinician will conduct during a consultation in order to assess a patient's risk for OCD characteristics.¹⁸ This survey is broken into ten different categories, five of them related to obsessions and five of them related to compulsions.^{18, 21} The Y-BOCS allows the medical professional to ask the patient a variety of questions related to aggressive obsessions, contamination obsessions, sexual obsessions, hoarding or saving obsessions, religious obsessions, obsession with the need for symmetry or exactness, miscellaneous obsessions, somatic obsessions, cleaning or washing obsessions, checking compulsions, repeating rituals, counting compulsions, ordering or arranging compulsions, hoarding or collecting compulsions, and miscellaneous compulsions.²¹ These categories are then further broken up into past and present so the patient can indicate whether they may have had these compulsions and obsessions in the past, if they currently feel them, or if they had them at all.²¹

While this is the main tool that clinicians may utilize in order to aid in the OCD diagnosis process, the guidelines that are set in the DSM-5 are also considered useful for diagnosis. When utilizing the DSM-5 for a potential OCD diagnosis, clinicians will look at the following criteria:²²

- A. Presence of obsessions, compulsions, or both. Obsessions are defined as recurrent and persistent thoughts, urges, or impulses that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress; the individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action. Compulsions are defined as repetitive behaviors (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly; the behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive.
- B. The obsessions or compulsions take more than 1 hour per day or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.
- D. The disturbance is not better explained by the symptoms of another mental disorder, such as a tic disorder

Individual OCD diagnoses can further be specified as having good or fair insight, poor insight, or absent insight/ delusional beliefs.²¹ An individual with good or fair insight may recognize that their OCD beliefs are definitely or probably not true. With poor insight, the individual thinks that the OCD beliefs are probably true. Individuals with absent insight and delusional beliefs are completely convinced that their OCD beliefs are true. The more that an individual is convinced that their OCD beliefs are true, they may experience a significant increase in OCD symptom exhibition as they become increasingly fearful that their obsessions and compulsions will prevent these OCD beliefs from occurring.

Another type of major anxiety disorder is Panic Disorder. Panic Disorder is often characterized by the presence of panic attacks.^{5, 11, 23, 24, 25, 26} These panic attacks have a rather quick onset, with the peak of the attack being just minutes after the beginning of the panic attack.^{5, 11, 24, 25} Panic attacks have been described as extremely intense and overwhelming feelings of impending doom, fear, discomfort, and dread.^{11, 24, 25} Some individuals have ever reported dissociating from their bodies during these panic attacks as a result of the intensity of the episode.⁵

On top of the overwhelming feelings that may come with the presence of a panic attack, some physical symptoms have also been reported to occur during these attacks. Some of these physical symptoms include an increased heart rate, increased respiration rate, chest or stomach pain, sensations of difficulty with breathing, weakness, dizziness, fatigue, sweating, chills or hot flashes (or both), tingling sensation in the hands, trouble concentrating, gastrointestinal issues, ringing in the ears, etc.^{5, 11, 24, 25, 26, 27}

Due to the immense amount of feelings that can occur during a panic attack, some individuals with severe cases of Panic Disorder may alter their lives in significant ways in order to prevent future panic attacks. Some of these life alterations may include being extremely selective in the individuals that one surrounds themselves with, avoiding a certain environment, ensuring that they are not alone during certain times of the day, etc. Some people with panic attacks that take these extra precautions may know and understand that these fears are not entirely logical, yet they might feel a decreased sense of anxiety over another panic attack occurring if these actions were not taken.

Certain situations (such as actions, environments, company, etc) may increase the likelihood that these panic attacks may occur.²⁵ The amount of stress that an individual is under may also induce the onset of these panic attacks.²⁴ Despite these environmental factors making the likelihood that a panic attack may occur, panic attacks may still have no obvious reason for occurring.

Panic Disorder is present in around 2-3% of individuals in the United States.^{9, 23, 27} This type of anxiety disorder is also about twice as likely to be presented in women than men.^{9, 23, 24, 25, 26} Most individuals with Panic Disorder begin getting panic attacks in early adulthood.^{23, 25} Despite most diagnoses being given around this age, children have been reported to exhibit “panic-like” states; 7 years of age is the typical onset for these episodes to occur.^{23, 25}

DSM-5 characterized panic attack diagnosis very clearly and is specific. The manual classifies panic attacks into two categories: expected and unexpected panic attacks.²⁶ Expected panic attacks are those associated with a specific fear while unexpected panic attacks have no apparent trigger or cue.²⁶ In order for anxiety to be officially classified as a panic attack four or more of the following symptoms:

- Palpitations, pounding heart, or accelerated heart rate
- Sweating
- Trembling or shaking
- Sensations of shortness of breath or smothering
- A feeling of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, lightheaded, or faint
- Feelings of unreality (derealization) or being detached from oneself (depersonalization)
- Fear of losing control or going crazy
- Fear of dying

- Numbness or tingling sensations (paresthesias)
- Chills or hot flushes

The fourth major type of anxiety disorder is Post-Traumatic Stress Disorder (PTSD). PTSD is characterized by traumatic and intense thoughts, memories, or dreams and avoiding things that remind you of the event, interruptions of sleep, and feelings of anxiety.^{28, 29, 30, 31} The initial event that causes an individual to develop PTSD can vary depending on the individual.

Rape is the most common source of PTSD; about half of the population that is a victim of rape will develop PTSD due to the traumatic event.⁹ Other intense and terrifying events that may cause PTSD may include car crashes, neglect in childhood, abuse, military combat, natural disasters, etc.^{28, 29} Lack of social support, increased stress, and other environmental factors can also influence the severity of the symptoms of PTSD one may experience.³¹ The development of PTSD may be caused by being directly involved in the situation or by witnessing the event as a bystander.^{30, 31}

The thoughts, memories, and dreams that come back after a traumatic event are referred to as flashbacks.^{28, 29, 30, 31} These flashbacks are extremely intense and may last for months or even years.^{28, 30, 31} They may also have a significant impact on an individual's life and has the chance to interfere with day-to-day functioning.

The intense flashbacks that one may experience can be caused by a variety of different triggers. Some of these triggers may include sights, smells, sounds, or thoughts that are connected to or remind an individual of the specific event that is the source of their PTSD.^{30, 31} PTSD affects 2.7-4% of individuals in the United States.^{9, 28, 31} Women are more likely to be affected than men.^{9, 28} Due to the fact that PTSD is developed after exposure to a highly traumatic event, PTSD can occur at any age.^{28, 31}

In order to aid in the diagnosis, the DSM-5 includes a very clear outline of the requirements for a diagnosis of PTSD. The following criteria are required:^{32, 33}

- A. Exposure to one of the following is required: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence. This exposure could have been obtained through direct exposure, witnessing the trauma, learning that a relative or close friend was exposed to trauma, or indirect exposure to aversive details of the trauma.
- B. The traumatic event is persistently re-experienced, in at least one of the following ways: unwanted upsetting memories, nightmares, flashbacks, emotional distress after exposure to traumatic reminders, or physical reactivity after exposure to traumatic reminders.
- C. Avoidance of trauma-related stimuli after the trauma in with trauma-related thoughts or feelings or trauma-related reminders.
- D. Negative thoughts or feelings that began or worsened after the trauma must have at least two of the following characteristics: inability to recall key features of the trauma, overly negative thoughts and assumptions about oneself or the world, exaggerated blame of self or others for causing the trauma, negative affect, decreased interest in activities, feeling isolated, or difficulty experiencing positive affect.

- E. Trauma-related arousal and reactivity that began or worsened after the trauma has at least two of the following characteristics: irritability or aggression, risky or destructive behavior, hypervigilance, heightened startle reaction, difficulty concentrating, or difficulty sleeping.
- F. Symptoms must last for more than one month.
- G. Symptoms are required to create distress or functional impairment.
- H. Symptoms must not be due to medication, substance use, or other illness.

The last major type of anxiety disorder is Social Phobia, which is also known as Social Anxiety Disorder (SAD). SAD is typically recognized by having an intense and overwhelming fear of social situations and settings.^{34,35, 36, 37, 38} SAD is different from being shy as symptoms and avoidance techniques related to SAD negatively impact an individual's life in social and professional settings.^{34, 35, 36, 37, 38, 39, 40} These feelings that impact one's life may be a result of embarrassment, self-consciousness, or concerns about being judged by others.^{34, 36, 37, 40} The avoidance actions may be selective and not occur constantly.^{34, 38}

In addition to the anxiety symptoms an individual with SAD may have, there are several physical symptoms that may be present as well; these symptoms may be exhibited through blushing, sweating, trembling, increased heart rate, forgetfulness, nausea, having a rigid body structure, difficulty making eye contact, increased feelings of consciousness, and avoidance of places where other people may be.^{34, 35, 36, 37}

SAD affects about 5-7% of the U.S. population.^{9, 39} The prevalence of SAD is the same in women as it is in men.⁹ The onset of symptoms typically begins around thirteen years of age or in childhood.^{35, 37, 38, 39}

In order to aid in the diagnosis of SAD, the DSM-5 has set up clean outlines for the criteria that are required for diagnosis. This manual states that in order for an individual to be eligible for a diagnosis of SAD, the following criteria need to be met:⁴¹

- A. A 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 embarrassing and humiliating.
- B. Exposure to the feared situation almost invariably provokes anxiety, which may take the form of a situationally bound or situationally predisposed Panic Attack.
- C. The person recognizes that this fear is unreasonable or excessive.
- D. The feared situations are avoided or else are endured with intense anxiety and distress.
- E. The avoidance, anxious anticipation, or distress in the feared social or performance situation(s) interferes significantly with the person's normal routine, occupational (academic) functioning, or social activities or relationships, or there is marked distress about having the phobia.
- F. The fear, anxiety, or avoidance is persistent, typically lasting 6 or more months.

G. The fear or avoidance is not due to direct physiological effects of a substance (e.g., drugs, medications) or a general medical condition not better accounted for by another mental disorder.

To summarize, there are several different anxiety disorders that may seem similar at first glance, but key differences make each anxiety disorder unique and allow for a specialized diagnosis. These specific differences that should be utilized during the diagnosis process by a medical professional are outlined in the DSM-5. Here is a generalized summary of the key difference between these anxiety disorder diagnoses.

- Generalized Anxiety Disorder (GAD): persistent and excessive anxiety or worry about even ordinary, routine activities. This worry is out of proportion to the actual circumstance, yet it is difficult to control and affects how you feel physically. It is often co-diagnosed with other anxiety disorders or depression.
- Obsessive-Compulsive Disorder (OCD): recurrent, unwanted thoughts (obsessions) and/or repetitive behaviors (compulsions). Performing these obsessions and compulsions may provide a temporary sense of relief; not performing them increases anxiety.
- Panic Disorder: occurrence of panic attacks, or episodes of sudden feelings of intense anxiety and fear or terror that have a rather quick onset for no obvious reason. A large range of unpleasant mental and physical symptoms may occur during these attacks. Concerns that these attacks will happen again or avoiding situations in which panic attacks have occurred may occur.
- Post-Traumatic Stress Disorder (PTSD): caused by a terrifying and traumatic event. This traumatic effect can be directly or indirectly experienced. PTSD will create flashbacks that can be triggered by reminders of the traumatic event. These flashbacks are present for at least one month and may affect daily life.
- Social Phobia (SAD) or Social Anxiety Disorder: high levels of anxiety, fear, and avoidance of social situations as a result of feelings of embarrassment, self-consciousness, and concern about being judged or viewed negatively by other people.

IMMUNE SYSTEM DISORDERS

Abnormalities within an immune system create the potential for the development of various allergic diseases, immunodeficiencies, and autoimmune disorders.³ Immune system disorder occurs when a component of the system over or under reacts to stimuli. This includes autoimmune disorders, where the body's antibodies attack self cells rather than targeting antigens.

There are two different types of immune systems found within the human body: the innate immune system and the adaptive immune system. The innate immune system serves as the first line of defense for the body. The innate immune system protects the body before an infection occurs. Parts of the body that are included epithelial barriers, mast cells, phagocytic

cells (neutrophils, macrophages), NK cells, the complement system, and cytokines. The innate system always functions properly in healthy individuals. Due to the simple nature of the innate immune system, this immune system is able to respond to any pathogens right away. Each time that the innate immune system reacts to a pathogen, it will react in the same fashion whether this infection is occurring for the first time or the one-hundredth time.

Inflammation is an example of an immune response that comes from the innate immune system. Inflammation is another word for swelling. Inflammation occurs in the human body when there is a reaction to an infection or a cellular injury. This reaction causes extravascular accumulation of plasma proteins and leukocytes. While inflammation is typically viewed with a negative connotation, inflammation exists as a protective function that is meant to control infections and promote tissue repair by encouraging the recruitment of immune cells to the site of injury or infection.

The other type of immune system that is present in the human body is the adaptive immune system. This immune system is much more complex and serves as the second line of defense for the body. The adaptive immune system will only need to react to an injury or infection if the innate immune system fails to eliminate all pathogens from the inside of the body. The adaptive immune system is composed primarily of B cells, T cells, and antibodies; these all play an important role in fighting infection.

When there is an issue with the adaptive immune system and the components are not functioning as properly as they should, autoimmunity may occur. Typically, B cells and T cells are able to bind to receptors on human cells and pathogens in order to differentiate what cells are part of the human body and which ones are foreign. However, when these cells are not created and coded properly, errors can occur. Either these cells will ignore pathogenic, non-human cells and fail to elicit an immune response or these cells will recognize human cells as pathogenic and foreign and elicit an immune response when one shouldn't have occurred.

Immune system disorders vary greatly in underlying mechanisms. Due to the complexity of the immune system and the human body as a whole, there are many errors that can occur that will lead to a near-infinite number of diseases and disorders. It is estimated that 4% of the world population has at least one immune system disorder and that between 3-8% of the United States population.^{42, 43, 44} Immune system disorders are about three times more prevalent in women than they are in men.^{42, 44} Immune system disorders may run in familial lines depending on the disorder and mechanisms that cause them.^{42, 44, 46} Some risk factors also exist when considering the likelihood that an immune system disorder will depend on some of these risks including environmental factors, previous infections, poor nutrition, etc.^{44, 45} Several different lines of research suggests that the incidence rate for immune system disorders may be increasing; despite many researchers suggesting this, there is not a clear reason why this rate is increasing.^{42, 46}

POTENTIAL LINKS BETWEEN ANXIETY DISORDERS AND IMMUNE SYSTEM DISORDERS

As different as immune system disorders and anxiety disorders may seem, current research is beginning to indicate that there could be a potential link between the two different types of disorders. This potential link between the two types of disorders is an extremely under-explored area of study. From the studies that are available, much of the research on anxiety disorders has been shown to have similar correlations to unconnected research on various immune system disorders. Although there has been little to no research conducted exploring the specific links between anxiety disorders and immune system disorders, these correlations in various other studies may be utilized in order to view possible connections and allow for future researchers and clinicians to begin the process of researching this link.

Existing research has noted that there may be a correlation between the amount of inflammation present in an individual and their mental and physical health. Inflammation is an immune response.⁴⁸ Inflammation is highly and positively associated with depression and anxiety; this means that as there is an increase in inflammation in the body, there has been a noted increase in anxiety-like symptoms.^{47, 48} While this may not always mean that the individual has an anxiety disorder diagnosis, this could have possible implications for when an individual with a noted anxiety disorder diagnosis has inflammation present.

The inflammation that is thought to be linked to anxiety disorders typically includes inflammation of the gut.^{48, 51} This inflammation is typically triggered by the cytokines (especially IL-6) and endotoxins that are released from the gut.^{47, 48, 49, 51} Due to the fact that various immune system disorders may increase the amount of inflammation in the body, this increased release of cytokines, such as IL-6, may cause a direct impact on the severity of feelings of anxiety.^{47, 48, 49} Although this has been the most researched connection between anxiety disorders and immune system disorders, there is not enough data available to run a meta-analysis to make a conclusive link between inflammation of the gut and anxiety disorders.

The biological composition of the gut microbiome may also play a significant role in the underlying pathway links of these disorders. Studies have shown that regulation of the gut microbiota exhibits a positive effect on anxiety symptoms.^{49, 52, 53, 54, 55} Different types of bacteria that have been identified in the gut have been shown to exhibit different effects on anxiety symptoms. Some bacteria, fungi, archaea, and protozoa identified in the gut are considered proinflammatory species as they aid in the promotion of inflammation in the gut.^{50, 51, 53, 54, 55} This means that depending on the composition of the gut microbiome, inflammation may increase. Due to the fact that inflammation has been shown to increase anxiety symptoms, these microorganisms present in the gut may contribute to the link between anxiety disorders and immune system disorders.

Another possible explanation for the links between these different types of disorders could be 5-HT correlation levels. 5-HT is also known as serotonin. Serotonin levels directly impact anxiety disorders; in order for an individual to have properly functioning mental processes, the chemical balance in the brain must be within normal range. When serotonin levels are measured outside of the normal range, a direct impact on emotions and mental health occurs. Due to this direct correlation, serotonin imbalances contribute to the development of anxiety

disorders according to various research studies.³⁴ As stated before, 5-HT levels also have been indicated to elicit a response of some kind towards the human immune system. These correlates may provide a possible lead to explore the links between anxiety disorders and immune system disorders.

Some medical conditions, including various immune system disorders, may cause physical sensations and pain that can induce anxiety; this induced anxiety may or may not be related to an anxiety disorder diagnosis. This is an important distinction that should be considered when a medical professional is considering a diagnosis of an anxiety disorder in a patient with an immune system disorder. A key factor that should be examined when making this diagnosis may be the duration of the anxiety-like symptoms. If symptoms were present before an individual had the symptoms of an immune system disorder, or if the symptoms persist for at least six months, then the individual may be a stronger candidate for an anxiety disorder diagnosis.⁶

METHODOLOGY

To start, a systematic review of available sources was conducted in order to aid in obtaining a general understanding of the existing knowledge regarding the link between anxiety disorders and immune system disorders. The initial preliminary articles were obtained by searching various scientific journals and analyzing primary literature that was found in relevant review studies. After reviewing each journal and study, only reliable sources were utilized in order to further access accurate information regarding the potential relationship between immune system disorders and anxiety disorders. These initial findings aided in the formation of the survey questions that were distributed to provide original research data.

An anonymous survey was then produced via Google Survey and distributed through word of mouth, various Canvas course announcements, student email campaigns, and social media. This distribution targeted college-aged students at The University of Nebraska at Omaha. The survey asked the following questions that allowed participants to provide information related to age, diagnosis of anxiety and immune system disorders, specification on which disorder had been diagnosed (if applicable), diagnosis of anxiety and immune system disorders within the family, age of familial diagnoses, whether medication is being taken for either type of disorder, and whether the medication treatment has been helpful in treating the symptoms of the disorder. After data collection, results were analyzed and compared to data from previous research in order to determine the validity of the potential link between anxiety disorders and immune system disorders. In order to further access the data that was collected, graphs were produced using the program Microsoft Excel.

A copy of the survey that was distributed can be found in the appendix.

RESULTS

As of May 8th, 2022, 119 responses were obtained from the distribution of the survey. The respondents who answered the survey questions ranged from 18- to 46-years of age; 69.7% of respondents were between the ages of 19 and 22 (Figure 1). 27 individuals, or 39.5% of respondents, indicated that they have been diagnosed with an anxiety disorder by a medical professional (Figure 2). The anxiety disorders diagnoses that were reported in the survey, from most to least prevalent, included GAD (22), panic disorder (6), social anxiety (5), panic disorder (5), OCD (4), PTSD (3), and situation anxiety (1). 6 individuals, or 5% of respondents, indicated that they have been diagnosed with an immune system disorder by a medical professional (Figure 3). The immune system disorders that were reported in the survey, from most to least prevalent, included Hashimoto's thyroiditis (3), type I diabetes (1), alopecia areata (1), asthma (1), and fibromyalgia (1).

Of the 119 respondents, 70 individuals (58.8%) reported that they have not been diagnosed with either an anxiety disorder or an immune system disorder (Figure 4). 42 individuals (34.5%) reported that they have been diagnosed with one or more anxiety disorders, but not with an immune system disorder (Figure 4). 2 individuals (1.7%) reported that they have been diagnosed with one or more immune system disorders, but not with an anxiety disorder (Figure 4). 6 individuals (5%) reported that they have been diagnosed with one or more anxiety disorders and one or more immune system disorders (Figure 4).

When individuals that reported being diagnosed with an anxiety disorder were asked whether they have taken medication to aid in the treatment for their anxiety disorder and if this medication was helpful in alleviating symptoms, 16 individuals reported that although they have an anxiety disorder diagnosis they are not taking any medications to aid in the relief of anxiety symptoms. 32 individuals reported taking medication to treat the symptoms associated with their anxiety disorder; 25 of these individuals reported that their medication has been helpful in alleviating their anxiety disorder symptoms while the other 7 individuals reported that their medication was not beneficial for them (Figure 5).

When individuals that reported being diagnosed with an immune system disorder were asked whether they have taken medication to aid in the treatment for their immune system disorder and if this medication was helpful in alleviating symptoms, 3 individuals reported that although they have an immune system disorder diagnosis they are not taking any medications to aid in the relief of immune system disorder symptoms. 5 individuals reported taking medications to treat the symptoms associated with their immune system disorder and that this medication has been helpful in alleviating their immune system disorder symptoms. No one had reported taking medication and that that medication is not beneficial in alleviating their immune system disorder symptoms (Figure 6).

Another survey question asked respondents about the anxiety system disorder and immune system disorder diagnoses that are present in their family history. 49 individuals (41.2%) indicated that they have no familial history of either an anxiety disorder diagnosis or an immune system disorder diagnosis (Figure 7). 40 individuals (33.6%) indicated that they have familial history of one or more anxiety disorder diagnoses but no history of an immune system

disorder diagnosis (Figure 7). 8 individuals (6.7%) indicated that they have familial history of one or more immune system disorder diagnoses but no history of an anxiety disorder diagnosis (Figure 7). 22 individuals (18.5%) indicated that they have familial history of one or more anxiety disorder diagnoses and one or more immune system disorder diagnoses (Figure 7).

To further access the familial history of the respondents, the next survey questions asked the respondents which age range best suits the age that their family has a history of obtaining their diagnoses of anxiety disorders. 14 individuals (11.8%) indicated that their family typically has a diagnosis for anxiety disorders between birth and the age of 16 years old (Figure 8). 37 individuals (31.1%) reported their familial anxiety disorder diagnoses to be between the ages of 16 and 25 years of age (Figure 8). 12 individuals (10.1%) reported their familial anxiety disorder diagnoses to be between the ages of 26 and 40 years of age (Figure 8). 3 individuals (2.5%) reported their familial anxiety disorder diagnoses to be between the ages of 41 and 55 years old. All other respondents indicated that they had no history of anxiety disorder diagnoses in their family (Figure 8).

The final survey question explored respondents' familial history of diagnoses for immune system disorders. 3 individuals (2.5%) reported that the immune system disorder diagnoses in their family occurred typically between birth and 16 years of age (Figure 9). 10 individuals (8.4%) reported that the immune system diagnoses in their family history occurred between 16 and 25 years of age (Figure 9). 8 individuals (6.7%) reported that the immune system diagnoses in their family history occurred between 25 and 40 years of age (Figure 9). 5 individuals (4.2%) reported that the immune system diagnoses in their family history occurred between 41 and 55 years of age. 2 individuals (1.7%) reported that the immune system diagnoses in their family history occurred between 56 and 70 years of age (Figure 9).

With the free-response option that was available to the respondents, a few individuals made note of a few conditions in their answers. For example, when subjected to the question "specify which type of anxiety disorder you have been diagnosed with", one individual wrote "Note: I have not actually been formally diagnosed yet, but it is likely that I do have social anxiety disorder (however I have not been formally diagnosed)". For this research, only disorders that have been officially diagnosed by a medical professional were included in this research so this response was omitted in the report of counts for social anxiety disorder counts. Another response indicated a similar response by stating "Generalized anxiety disorder (I think)". This response was also omitted in the disorder indication counts because they indicated that they have not had the diagnosis by a medical professional.

25 individuals reported only being diagnosed with one anxiety disorder while 8 individuals listed more than one anxiety disorder diagnosis. When asked to indicate what types of anxiety disorder diagnoses have been obtained, some individuals also indicated a disorder that is not an anxiety disorder; examples of these responses include depression, ADD, and ADHD. These responses were not included in any data count as they are deemed irrelevant to this specific study.

DISCUSSION

According to the survey results, most individuals that have been diagnosed with an immune system disorder have also been diagnosed with an anxiety disorder. A smaller proportion of the respondents reported being diagnosed with an immune system disorder but not an anxiety disorder than the number of respondents that reported being diagnosed with an anxiety disorder but not an immune system disorder. This correlation indicates that there is a high indication that there is a link between anxiety disorder and immune system disorders.

The survey that was distributed for data collection contained two different questions regarding medications and the medicinal impact on anxiety disorder and immune system disorder side effects. Due to a severe shortage in articles and research that discuss the presence of the immune system disorder and anxiety disorder link in relation to medication treatments, these questions were disregarded as no links were able to be drawn. More conclusive research will need to be conducted that determines the link between anxiety disorders and immune system disorder before the impact of medicine should be included in the research; this may also make the data and relationship for this link to be more clear as well by narrowing the amount of variables that can alter the data.

As previously mentioned, the mechanisms that result in an immune system disorder can greatly vary depending on the body system that the immune system is impacting. The pathways that control immune system disorders essentially vary significantly more than the mechanisms that control the various forms of anxiety disorders. This means that in order to determine whether a link exists, the most efficient way to study the potential links would be to study the relationship of each individual immune system disorder to anxiety disorders as a whole. In order to follow this logic, a breakdown of each immune system disorder, as well as an explanation of the possible links to anxiety disorders, are listed below.

ALOPECIA AREATA

Alopecia areata is an autoimmune system disorder that leads to hair loss.^{56, 57, 58, 59, 60, 61, 62, 63, 64, 65} Alopecia is the medical term for “bald” while areata means “patchy”; this indicates that there are various types of alopecia depending on the severity of the hair loss.⁶⁰ This hair loss typically appears as a bald spot as a result of the immune system promoting an unnecessary immune response on an individual’s hair follicles as a result of overactive T cells creating inflammation that does not have any benefit to the body.^{56, 58, 59, 60, 61, 62, 63, 64} This immune response makes the hair follicle shrink too small that hair production rates are decreased dramatically. Some individuals may have a chronic consistent hair loss while other individuals experience chronic but occasional hair loss.^{58, 59, 61} Changes may also occur in finger and toenails as human nails and hair have similar compositions.^{59, 60, 61, 62, 63, 64} When nails are affected, an individual that has alopecia areata may exhibit more dents, ridges, decrease in strength, redness around the nail bed, and other imperfections.^{59, 60, 61, 62, 63}

Symptoms such as hair loss may start to develop at any age throughout the human lifespan, but most commonly these symptoms appear in either childhood or in teenage years.^{57, 59, 60, 61, 62} There are no noted differences in the prevalence rates in women and men.^{59, 61, 63} There are also no noted differences in the prevalence rates between different ethnic groups.^{60, 61} Patients that also have thyroid disease, vitiligo, and atopic eczema have shown an increased risk of developing alopecia areata.^{59, 62, 64}

Although the exact cause of this condition is not entirely known, the most plausible reasoning behind the development of alopecia areata is that the disorder is hereditary; one in five individuals who exhibit symptoms of this disorder have also had a family member who has been diagnosed with this disorder as well.^{59, 60, 61, 62, 63} There has also been a total of eight susceptibility genes that have been identified in individuals with this disorder.^{59, 60, 61, 62} Few chromosomal abnormalities have been noted at higher rates in individuals that have been diagnosed with alopecia areata as well.^{59, 60, 61, 62}

While genetic links have been seen through gene mapping and family trees, another possible link between alopecia areata and anxiety has been suggested that we are not able to see directly: stress. Many studies have exhibited an increase in stress levels in individuals with this condition have been seen through an increased level of 5-HT.^{57, 65} Many articles and publications indicate that this is an area of study that should receive more attention for this disorder.

FIBROMYALGIA

Fibromyalgia is a chronic disorder that causes extreme physical pain throughout the body.^{66, 67, 68, 69, 70} The disorder affects the musculoskeletal system by increasing the sensitivity of the neurons and chemical signals of the brain and spinal cord.⁶⁶ The parts of the musculoskeletal system that is targeted includes the muscle, ligaments, and tendons. This increase in neuronal sensitivity is what leads to the higher perception of pain throughout the body. Symptoms other than the pain sensation also exist. Other symptoms may include fatigue, sleep complications, emotional changes, gastrointestinal issues, increased menstrual pain, and "fibro fog".^{66, 67, 68, 69} "Fibro dog" can be defined as an impairment in the ability to focus, pay attention and concentrate on a variety of mental tasks.^{66, 68, 69}

Symptoms of fibromyalgia may gradually get worse over a lifespan and have no known exact point of origin; in other cases, fibromyalgia may develop after a traumatic physical event occurs.^{ADD} These symptoms may worsen during certain times of the day as well, such as mornings or evenings.⁶⁸

Fibromyalgia is not an immune system disorder, but it does have a direct impact on the immune system by causing various irregularities; due to its effects on the immune system, this disorder may also be worth exploring when considering disease links to anxiety disorders. In fact, anxiety disorder diagnosis has been a noted risk factor for the development of fibromyalgia.^{66, 67, 68, 69, 70} Other risk factors include poor sleep habits, genetics, lack of exercise, repetitive injuries, severe infections, the presence of migraines, tension headaches, IBS, temporomandibular joint (TMJ) disorders, irritable bowel syndrome, anxiety and depression.^{66, 67}

Fibromyalgia affects about 2% of the population in the United States.^{67, 70} Women are also about twice as likely to get the disorder than men.⁶⁷ While this disorder has been presented in children, most cases of fibromyalgia occur during the middle ages of life.^{67, 68, 69}

Relaxation and stress-reducing measures have been shown to decrease the physical symptoms of fibromyalgia.^{67, 68, 69} This may provide additional implications for the connection of this immune system-affecting disorder to provide a clearer answer on the links between anxiety disorders and immune system disorders.

ASTHMA

Asthma is a condition that is caused by an overactive immune system. Research has been conducted to determine if asthma can be considered an autoimmune disorder or if the condition may be an inflammatory disease that worsens by the immune system; mixed results and conclusions have been found.^{71, 72, 73, 74} Whether asthma is considered an autoimmune disorder or an inflammatory disease, there are obvious links to the disorder and the immune system. This disorder is indicative of swollen airways and extra mucus production within the lungs.⁷⁵ The inflammation will also contribute to the walls of the lungs to grow thicker.⁷⁶ Occasionally, this inflammation or swelling and mucus build-up causes an asthma attack. These asthma attacks are defined as periods of wheezing, shortness of breath, chest tightness, and coughing.^{74, 76} Asthma attacks can be mild, or they may be severe to the point where it impacts daily life; this most severe cases may even require hospitalization.⁷⁴

Asthma attacks are often associated with a trigger. Some environmental factors, such as exposure to allergens, an abundance of physical activity, various medications, poor air quality, extreme amounts of stress, and various infections.⁷⁵ The common cold is one of the most noted triggers for asthma attacks to occur.^{74, 75, 77}

Various risk factors have been presented in literature that have been thought to contribute to the likelihood that one may develop severe asthma. Some of these risk factors include genetic links, presence of allergies, obesity, exposure to second hand smoke, sex, occupational hazards, administration of certain beta blocker medications, and occurrence of viral infections.^{74, 75, 77}

Around 8% of the United States population has obtained a diagnosis of asthma.⁷⁸ Individuals that have been diagnosed with some form of allergies make up a significant portion of the individuals who also have asthma.^{75, 77} Body mass has also been noted to have an impact on the severity and presence of asthma as obesity is correlated with an increase development for the disorder.⁷⁵ African Americans and Puerto Ricans have reported having an increased risk in developing asthma; these same groups of individuals also have an increased risk of death from asthma-related causes.⁷⁵ In childhood, boys are more likely to experience asthma-like symptoms than girls; in teenage and adult years, women are more likely to experience asthma-like symptoms than men.⁷⁵ Due to the fact that environmental triggers such as chemicals, dusts, molds, pollen, etc have been identified, individuals who have occupations with a high level of exposure to these triggers have an increased likelihood of developing asthma.

To further indicate that asthma is strongly linked to the immune system and the anxiety both, one may look at the effectiveness of immunosuppression medications as treatment for asthma patients. The inflammation caused by asthma is often suppressed by these drugs, indicating that the immune response of inflammation does worsen the condition. On top of this, anxiety has been shown to be a risk factor for asthma.⁷⁵ This may be due to the fact that asthma and anxiety increase when an individual with the disorder is experiencing a heightened level of stress. This link, however, is still severely understudied and more research will need to be conducted on the links between anxiety and asthma in order for the scientific community to draw conclusive links on the topic.

HASHIMOTO'S THYROIDITIS

Hashimoto's Thyroiditis is the most common type of hypothyroidism.⁷⁹ This means that the thyroid gland, which is responsible for secreting a large variety of hormones in the human body, underproduces hormones. This underproduction of thyroid hormones is a result of inflammation of the thyroid gland.

This disorder is indicative of weight changes, mood changes, severe fatigue, etc.⁷⁹ A high prevalence rate of individuals with Hashimoto's Thyroiditis.^{80, 82} 4-13% of the United States population has Hashimoto's Thyroiditis.⁸¹ This disorder has been diagnosed in more women than men.⁸¹ After the age of 6, Hashimoto's Thyroiditis is the most commonly diagnosed thyroid disorder among the United State's population.⁸⁰

This inflammation serves as a link between Hashimoto's Thyroiditis and the immune system. Hashimoto's Thyroiditis is considered an autoimmune disorder.⁸⁰ The inflammation associated with this disease occurs due to the body's white blood cells attacking the thyroid gland, thinking that this is a foreign cell or object even though it is indeed part of the body.

This disorder is severely understudied as a whole and before this disorder can be utilized to assess the risks between anxiety disorders and the immune system, more research will need to be conducted on the autoimmune system disorder itself. Although some research has indicated that anxiety is a risk factor for Hashimoto's Thyroiditis, other research lists anxiety as a symptom of the Hashimoto's Thyroiditis; this means that some researchers are arguing that anxiety is contributing to the worsening of the disease while others believe that the symptoms of Hashimoto's Thyroiditis is actually a result of the disorder itself so that those individuals will not require an additional diagnosis of an anxiety disorder.^{82, 83}

TYPE I DIABETES

Type I Diabetes is a chronic, autoimmune disorder in which the pancreas does not produce any or enough insulin for the body.⁸⁵ This lack of insulin production originates from the absence of or destruction of beta cells that are found in the pancreas. Pancreatic beta cells of the islet of Langerhans are the cells that produce insulin.⁸⁵ Type I Diabetes is an autoimmune disorder because the body's immune system will recognize these beta cells as foreign and attack and destroy these pancreatic cells.⁸⁶

Insulin is vital to ensure that an individual with this disorder stays alive as the insulin controls the amount of glucose, or sugar, in the blood. These blood sugar levels need to stay within a certain range in order for the body to properly function. This means that individuals that have Type I Diabetes are required to take insulin injections everyday and monitor their blood sugars every time they eat or don't eat for long periods of time.⁸⁶

Some symptoms of diabetes, other than blood sugar levels, may include increased thirst, frequent urination, extreme thirst and hunger, unexpected weight loss, irritability/ mood changes, fatigue, weakness, and blurred vision.^{85, 86} These symptoms may vary between individuals who are affected by Type I Diabetes; the severity of the symptoms may also be affected by the blood glucose levels and how out-of-range they may be.

An individual may be born with Type I Diabetes but the disorder may also develop in childhood or early adulthood. Although the risk factors for type I diabetes development are not as well-known as the risk factors for other types of diabetes, some suggested risk factors include genetics, age, and ethnicity.^{85, 86} More research will need to be conducted on the underlying mechanisms that contribute to the development of Type I Diabetes in order for more conclusive risk factors to be identified.

0.03% of individuals within the United States have been diagnosed with Type I Diabetes; the worldwide prevalence of this disorder is much higher though with 2-5% of individuals worldwide having this disorder.⁸⁷ While there are no studies that indicate that women or men show a higher prevalence of Type I Diabetes, it has been noted that women, especially those who are pregnant, have an increased risk of developing anxiety as a result of their Diabetes.⁸⁸

Especially when blood glucose levels are not within normal range, feelings of anxiety can be presented in individuals with Type I Diabetes. Many researchers have identified that Type I Diabetes causes a significant increase in the risk of developing anxiety-like symptoms.^{88, 89} More research may need to be conducted in order to determine if Type I Diabetes aids in the development of an anxiety disorder or if anxiety-like symptoms occur as a result of the diabetes itself. Determining the strength of the link between anxiety and Type I Diabetes will provide further support for researchers to draw conclusions about the links between anxiety disorders and immune system disorders.

CONCLUSION

There are several possible leads available that can be explored to explain the strength of the link between anxiety disorders and immune system disorders. Various potential explanations for links between these types of disorders were found during preliminary research of existing data that could be the focus of future studies as well. For example, several reports have been made suggesting a link between the gut microbiome to anxiety disorders and also a link between the gut microbiome and immune system disorders. Research has also shown correlations between anxiety symptoms and 5-HT levels. Although these explanations may seem promising explanations, much more research will need to be conducted in order to officially and confidentially determine the underlying mechanisms that may link these types of diseases.

A majority of the respondents that responded to the survey that was conducted reported being aged between 19 and 22 years of age. This indicates that these results mostly represent the young adult population. Due to the fact that the majority of survey respondents were in their early adulthood years, there may be a higher number of undiagnosed individuals in this population. A high percentage of individuals that have anxiety disorders may not get diagnosed with the correct anxiety disorder until they are older than 22 years of age due to inaccessibility to the resources that would be required for a diagnosis. This is especially harmful to the data available that would be needed to be analyzed to access this potential link because lower economic status serves as an additional risk factor for anxiety disorder prevalence.

About half of the individuals who have obtained an anxiety disorder diagnosis in the United States have waited for 2 or more years before being officially diagnosed with what psychiatrists then believe is the correct diagnosis.¹⁰ Some young adults in the survey also may not be willing or knowledgeable enough about anxiety to realize that they need to be considered for this anxiety disorder diagnosis, likely in part due to the negative stigma that is attached to anxiety disorders in modern society today. This could further implicate that the amount of diagnoses of anxiety disorders is severely underestimated. After accounting for the diagnoses that may not be present in case databases, the link between anxiety disorders and immune system disorders may show a stronger correlation than the current data may suggest.

During the survey results, one respondent indicated that “Note: I have not actually been formally diagnosed yet, but it is likely that I do have social anxiety disorder (however I have not been formally diagnosed)”. This further indicates that the number of individuals that reported having an anxiety disorder in the survey and in other research may actually be an underestimation of individuals that suffer from an anxiety disorder. Taking this into consideration would also indicate that the possible link between anxiety disorders and immune system disorders may be stronger than the data that is available may lead researchers to believe.

Both immune system disorders and anxiety disorders can develop at any point in one’s life. This means that the same exact survey that was conducted could be redistributed in about twenty years and different data and conclusions may be met based on the differing results that may be obtained. As individuals age, the immune system may slowly decrease in efficiency,

increasing the likelihood that an immune system disorder may occur as well. This would also lead to a stronger link than the current data may lead researchers to suggest.

With the research and data that has been presented between the preliminary research and the survey results, a possible link can be observed between anxiety disorders and immune system disorders. However, the data presented does not suggest whether there is a bidirectional relationship present between these two types of disorders. In other words, this data cannot prove that anxiety disorders influence anxiety disorders in the same manner that anxiety disorders may impact the present immune system disorder. This also means that no conclusion can be drawn on whether one of these types of disorders actually causes the other, or if they both need to already exist in order to have any effects on each other.

Due to the fact that correlation does not always suggest causation, there is a serious lack of sufficient research that would be needed in order to establish a link between anxiety disorders and immune system disorders. For a more comprehensive view of this relationship, more studies will need to be conducted with a larger sample size. Future research may also benefit from focusing on various age groups rather than combining all of the data from a population into one survey; this would also show whether age may impact the strength of the relationship between anxiety disorders and immune system disorders, especially since the prevalence of certain immune system disorders is much more common in older populations compared to the younger ones.

FUTURE RESEARCH DIRECTIONS

As stated before, the idea that anxiety disorders and immune system disorder mechanisms are linked is severely under-explored in the scientific field. Research has examined the levels of 5-HT in the body and its correlation with anxiety disorders. Other research has been conducted that has provided some insight on the correlation between 5-HT and the severity of immune system disorders. However, no studies have taken the 5-HT data into consideration while examining both anxiety disorder severity and immune system disorder severity. In order to provide the most accurate correlations, future research should examine the 5-HT levels in individuals with one specific immune system disorder and anxiety disorders as a whole; this will create more focused research as the underlying mechanisms for various immune system disorders can vary more greatly than the molecular pathways that are involved in anxiety disorders.

The importance of the gut microbiome and its effects on various aspects of health in the human body has become more emphasized in recent years of research. Despite this newly highlighted topic gaining importance in the scientific field, there has been no inclusive research on the concurrent effects of the gut microbiome on anxiety and immune systems. Compared to the amount of research that has been conducted on the effects of the gut microbiome on immune system processes, not much research has been conducted on the correlations in gut microbiome health with the prevalence of immune system disorder diagnoses. Even less research has been

conducted on the correlations between gut microbiome health and the prevalence of anxiety disorder diagnoses. Future research would benefit from emphasizing the relationship of the gut microbiome to individuals that have at least one anxiety disorder diagnosis, at least one immune system diagnosis, and even individuals that may present at least one anxiety disorder diagnosis and at least one immune system diagnosis.

Age groups-specific data may be collected in the future, allowing researchers to create a more comprehensive view of whether the links between anxiety disorders and immune system disorders increase or decrease in strength with increased age. Along with focusing data on subgroups like age, it would also be extremely beneficial to explore the sex differences. Anxiety disorders are much more common in women so it may be beneficial to explore whether this potential link between anxiety disorders and immune system disorders varies in strength between the two sexes.

In cross-cultural comparisons, prevalence rates of anxiety disorders are highly variable.^{1,11} Future research may be able to focus on whether various cultures have variable rates of immune system disorders and anxiety disorders; comparing these varying rates of each disorder to similar and different cultures may provide insight on whether a cultural influence is able to influence the strength of the relationship between anxiety disorder and immune system disorder links.

LIMITATIONS OF THIS STUDY

There are some limitations that come with this review. First, this survey has grouped all age groups together; eliminating the factor of age from this study provided a decent sense of general correlations, but this relationship may vary greatly in strength throughout a lifespan. To further improve this aspect of the data, it would have been helpful to be able to look at the percent of anxiety disorder diagnoses as broken down between each age group. This limitation is aided slightly by considering the familial history data.

Although the target audience of this was the student population of the University of Nebraska at Omaha, the age range to take this survey was not limited to young adults; while the survey was spread to primarily college students, anyone with the survey link may have given a response. As a result, the age range of all participants varied between 18 and 46 years of age. The survey results may be also skewed as college students are typically experiencing higher stress levels than normal towards the end of the semester. My survey also asks for diagnoses that are not self-diagnosed, but instead have been confirmed by a medical professional. Some individuals have anxiety and immune system disorders that may be underlying and not diagnosed by a medical professional. In order to get more confident results, future studies may have a medical professional do an assessment of participants to ensure that correct diagnoses and responses have been obtained.

SUPPLEMENTAL FIGURES

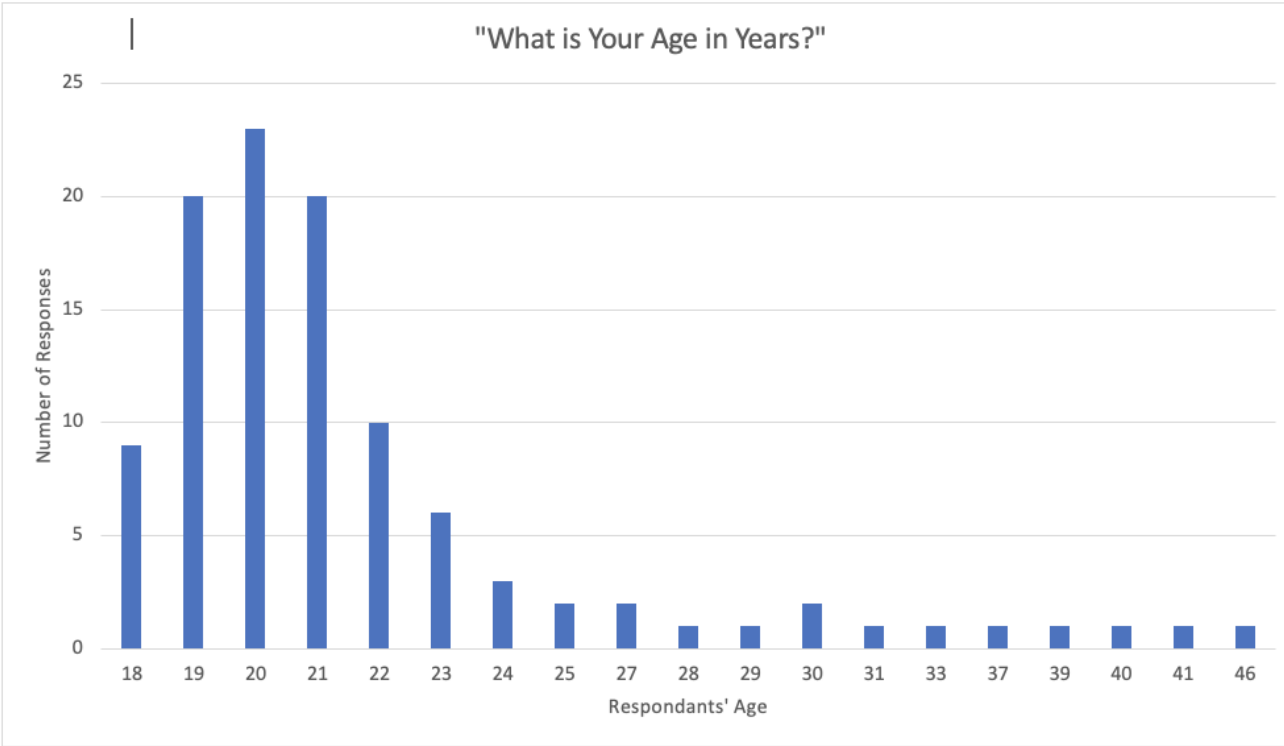


Figure 1. "What is your age in years?" Respondents answered that as of the day that they filled out this survey, their age was 18 (9), 19 (20), 20 (23), 21 (20), 22 (10), 23 (6), 24 (3), 25 (2), 27 (2), 28 (1), 29 (1), 30 (2), 31 (1), 33 (1), 37 (1), 39 (1), 40 (1), 41(1), 46 (1).

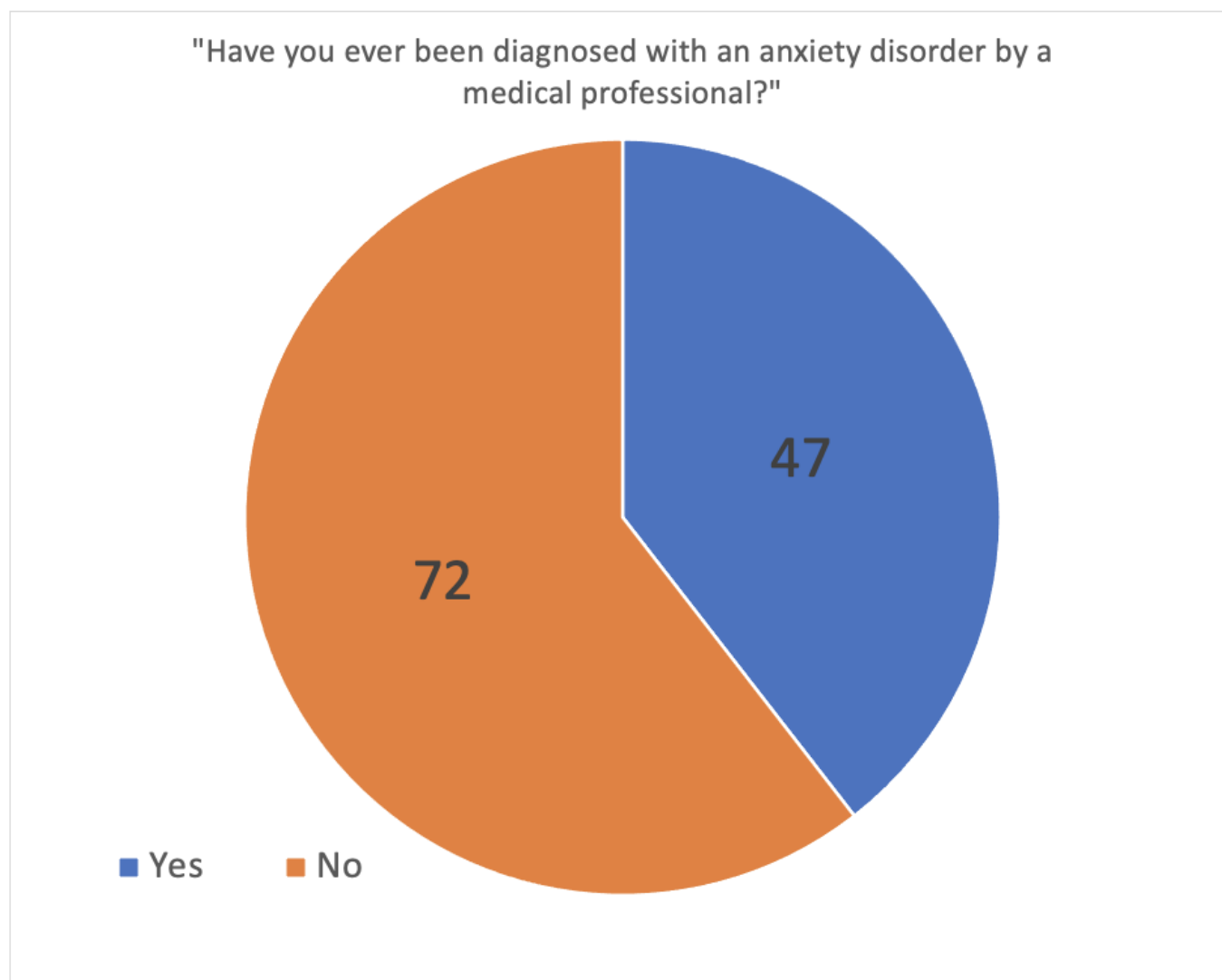


Figure 2. "Have you ever been diagnosed with an anxiety disorder by a certified medical professional?" 72 (60.5%) of individuals reported that they have not been diagnosed by an anxiety disorder. 47 (39.5%) of individuals reported that that they have been diagnosed with at least one anxiety disorder.

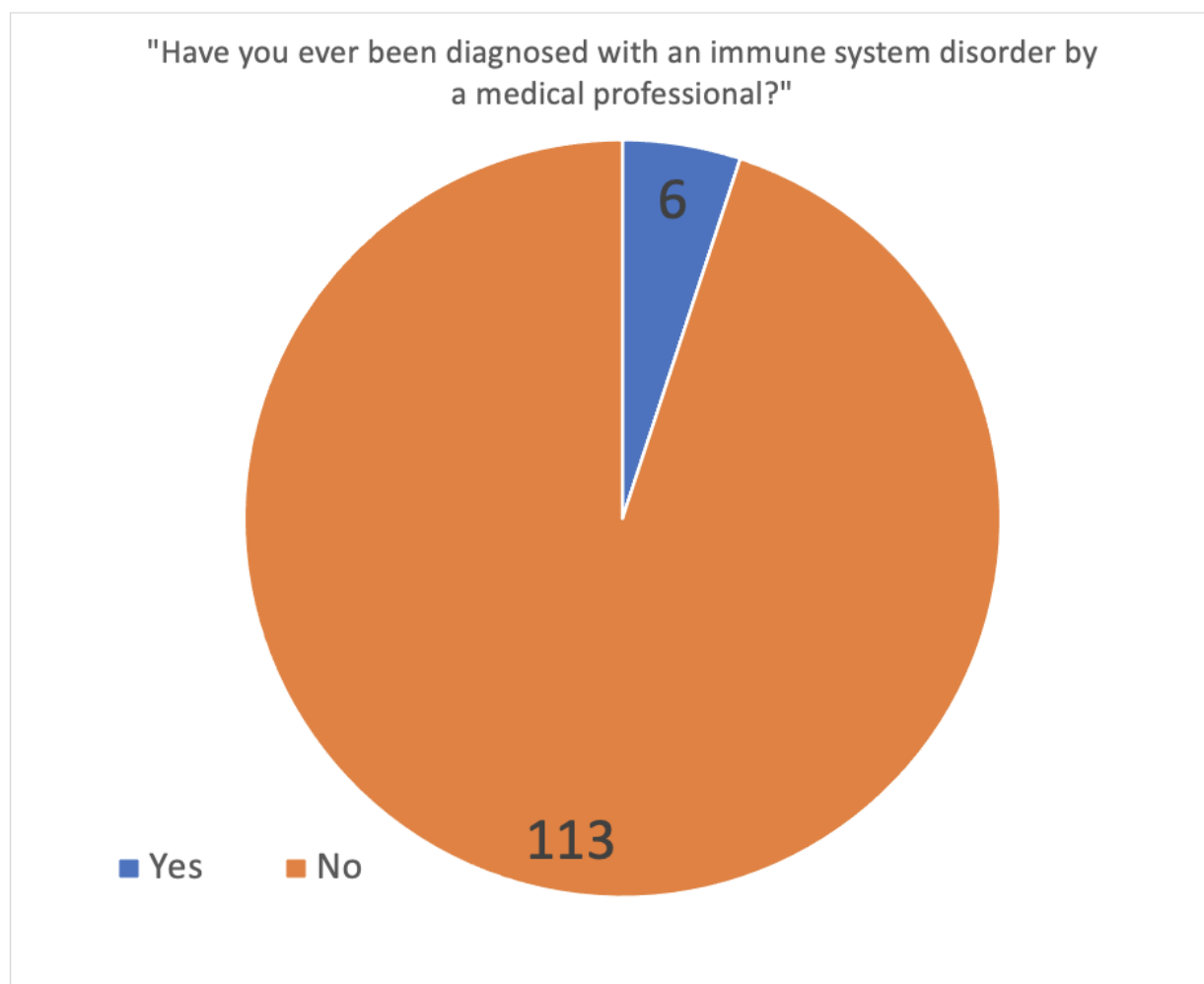


Figure 3. "Have you ever been diagnosed with an immune system disorder by a medical professional?" 113 (95%) of individuals reported that they have not been diagnosed with an immune system disorder. 6 (5%) individuals reported that they have been diagnosed with at least one immune system disorder.

Indication of Anxiety Disorder and/or Immune System Disorder in Self

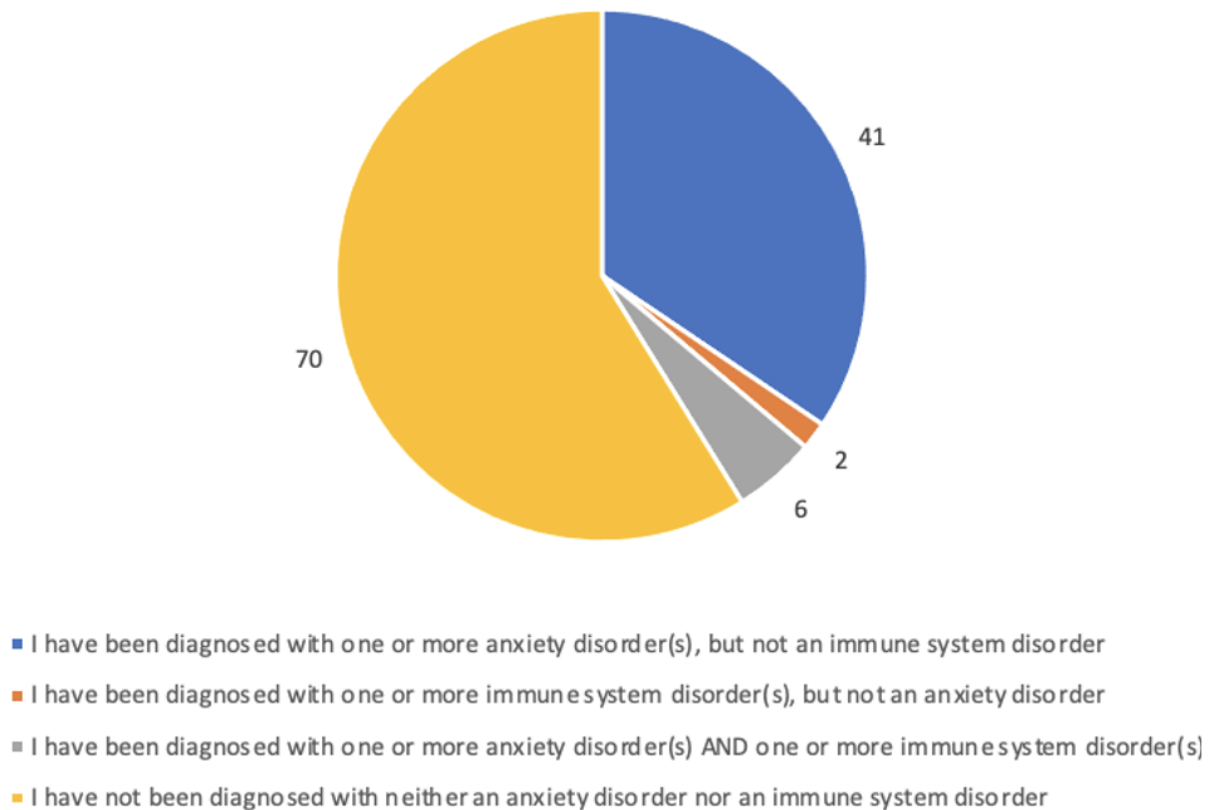


Figure 4. Respondents were asked to choose the statement that most accurately described themselves. 70 (58.8%) of individuals reported that they have not been diagnosed with neither an anxiety disorder nor an immune system disorder. 41 (34.5) of individuals reported that they have been diagnosed with at least anxiety disorder, but not with an immune system disorder. 2 (1.7%) of individuals reported that they have been diagnosed with one or more immune system disorder, but not with an anxiety disorder. 6 (5%) of individuals reported that they have been diagnosed with at least one anxiety disorder AND at least one immune system disorder.

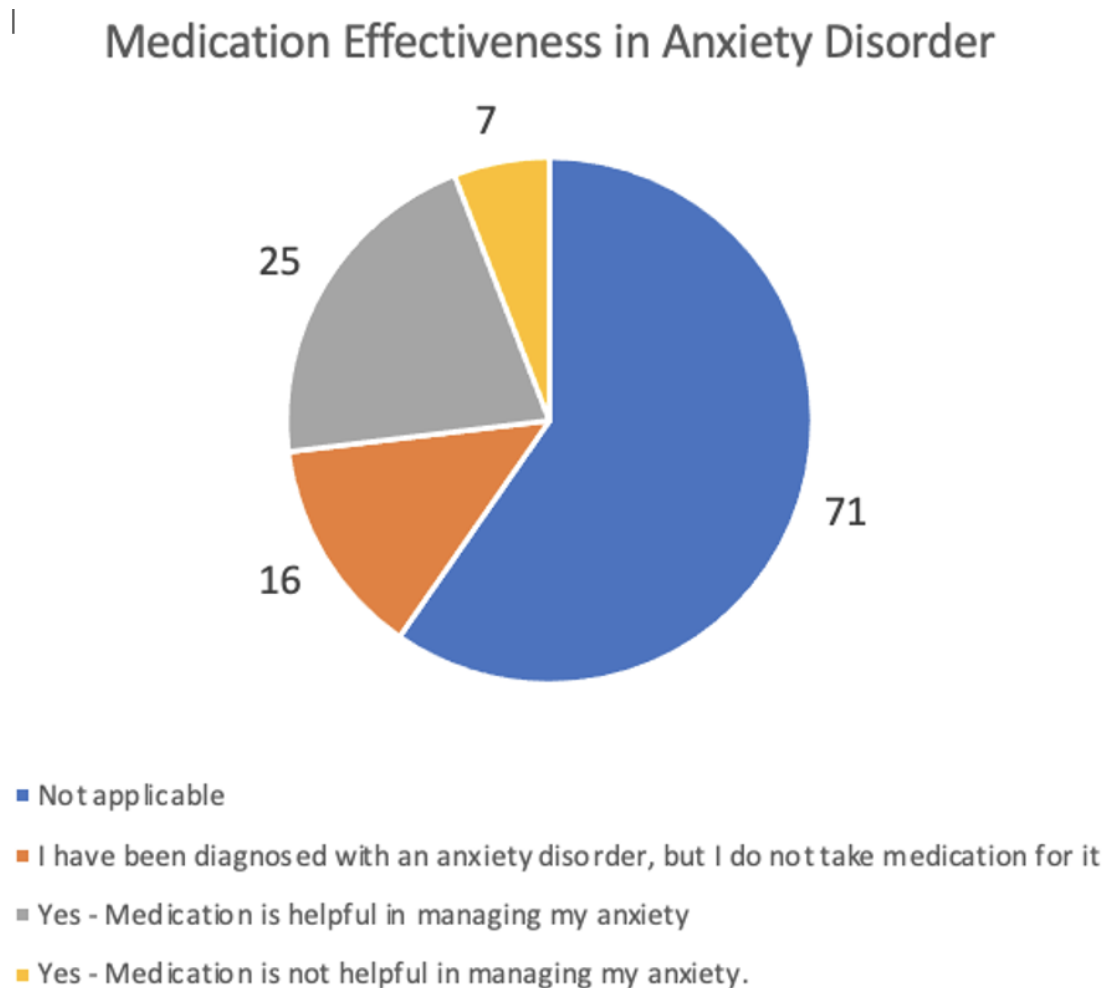


Figure 5. "If you indicated that you have been diagnosed with an anxiety disorder, do you current or have you taken medication to aid in controlling your anxiety disorder symptoms? If applicable, do you feel that medication is beneficial to managing your anxiety?" 71 (59.7%) of individuals have not been diagnosed with an anxiety disorder so they indicated that this question was not applicable to them. 16 (13.4%) of individuals have been diagnosed with an anxiety disorder but they do not take medication to aid in symptom management. 25 (21%) of individuals reported that they have an anxiety disorder diagnosis, that they take medication, and that the medication is helpful in managing their anxiety symptoms. 7 (5.9%) of individuals reported that they have an anxiety disorder diagnosis, that they take medication, and that the medication is not helpful in manage their anxiety symptoms.

Medication Effectiveness in Immune System Disorders

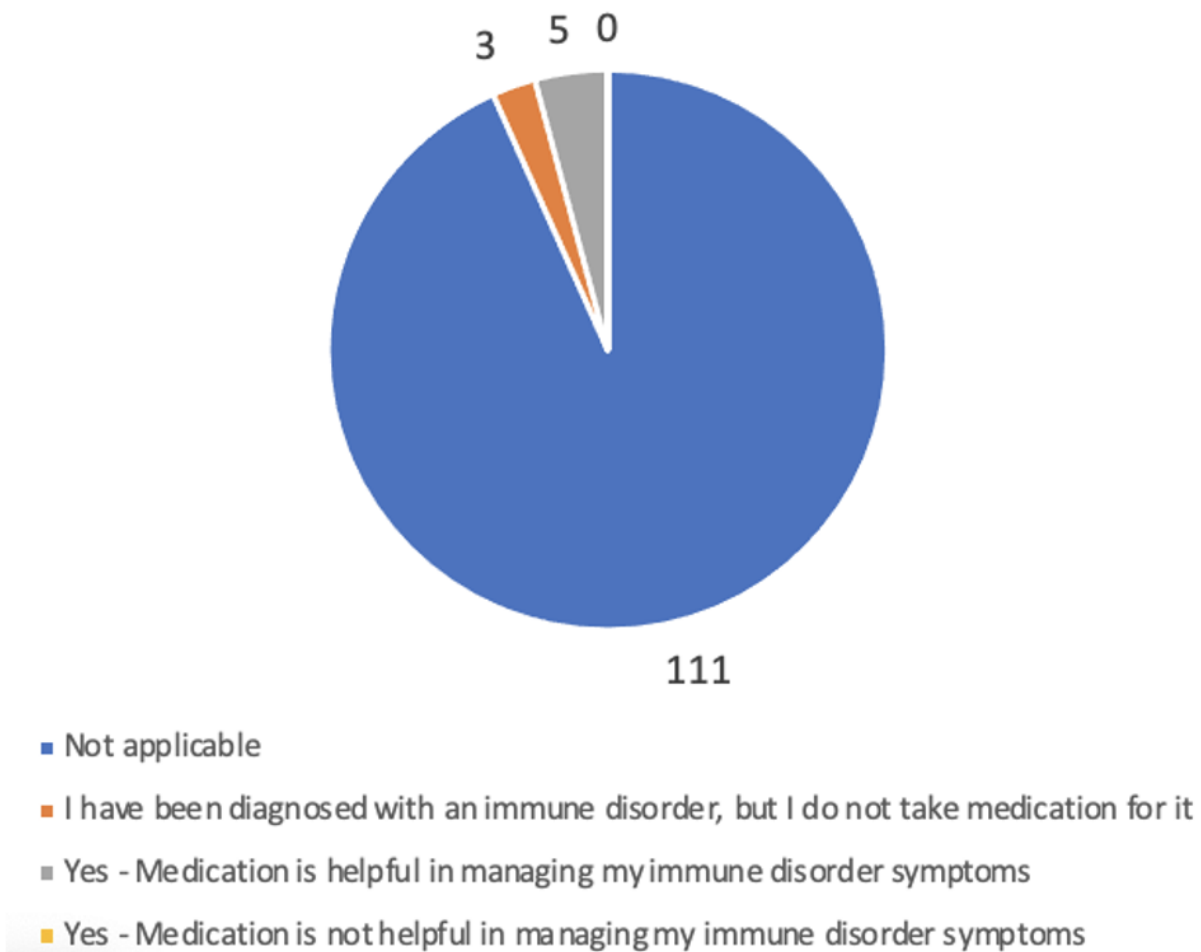


Figure 6. “If you indicated that you have been diagnosed with an immune system disorder, do you currently take medication or have taken medication in the past to aid in controlling your immune system disorder symptoms? If applicable, do you feel that medication is beneficial to the management of your immune system disorder?” 111 (93.3%) of individuals have not been diagnosed with an immune system disorder so they indicated that this question was not applicable to them. 3 (2.5%) of individuals have been diagnosed with an immune system disorder but they do not take medication to aid in symptom management. 5 (4.2%) of individuals reported that they have an immune system disorder diagnosis, that they take medication, and that the medication is helpful in managing their symptoms. No individuals reported that they have an immune system disorder diagnosis, that they take medication, and that the medication is not helpful in manage their anxiety symptoms.

Familial History of Anxiety Disorder and Immune System Disorder Diagnosis.

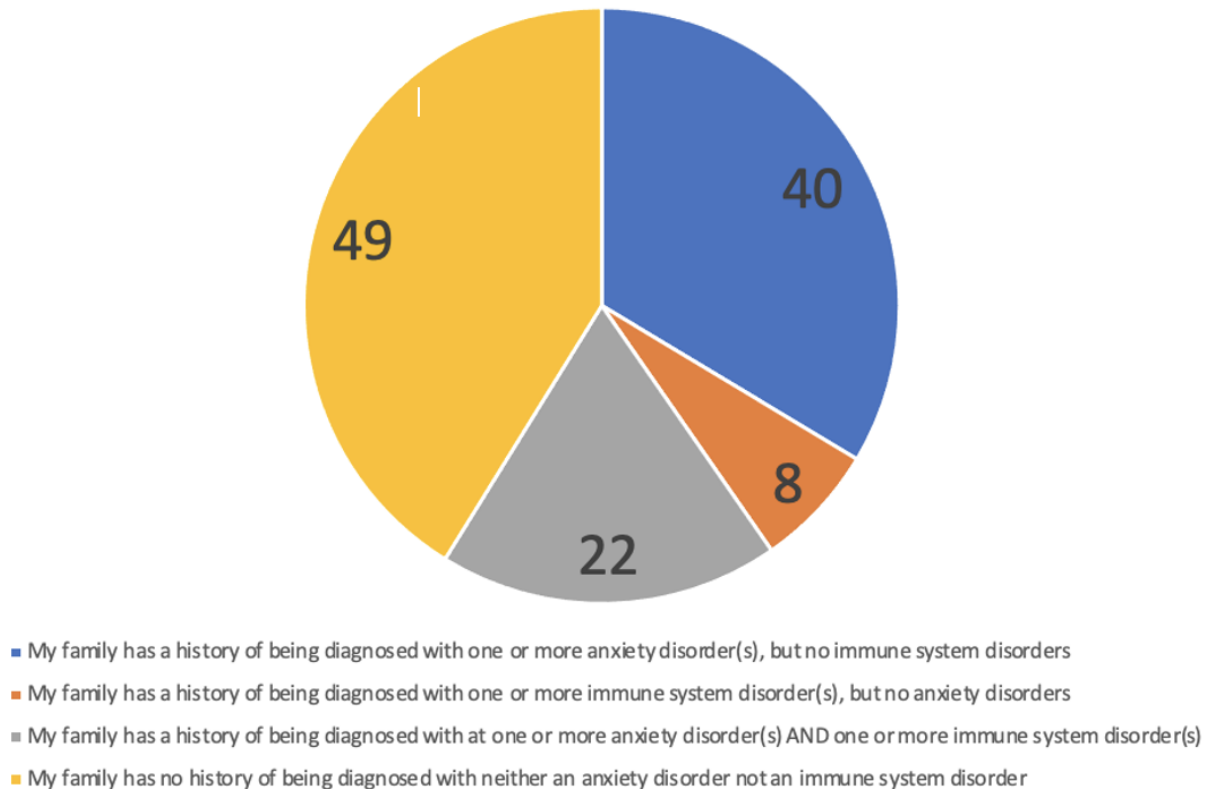


Figure 7. "Please select the statement that generally describes your family history, not including yourself." 40 (33.6%) of respondents indicated that their family has a history of anxiety disorder diagnoses, but not immune system diagnoses. 8 (6.7%) of respondents indicated that their family has a history of immune system diagnoses, but not anxiety disorder diagnoses. 22 (18.5%) respondents indicated that their family has a history of being diagnosed with at least one anxiety disorder AND at least one immune system disorder. 49% (41.2%) of respondent indicated that they have no familial history of neither anxiety disorders nor immune system disorders.

Familial Age When Anxiety Disorder Diagnosis was Obtained

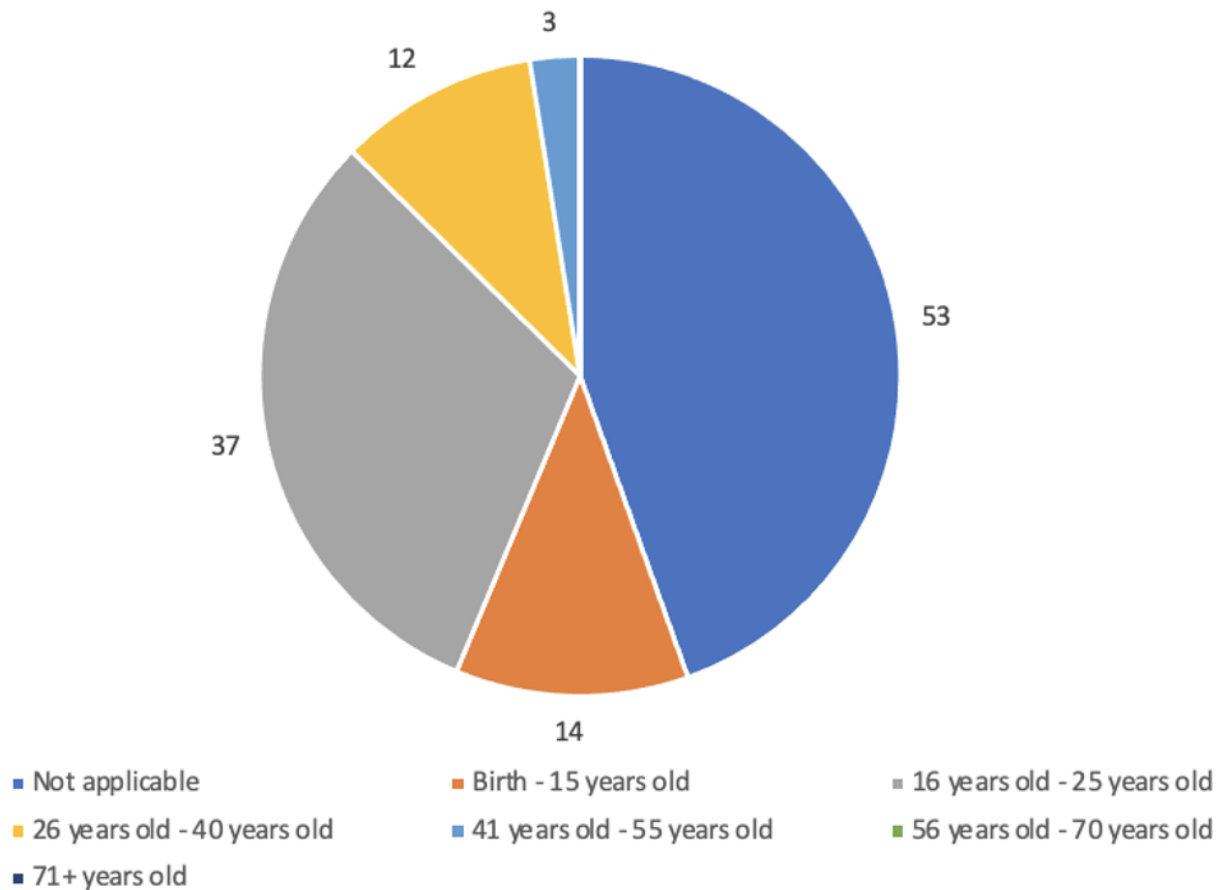


Figure 8. "If applicable, which age range best suits the age that you and your family has obtained a diagnosis for their anxiety disorder?" 53 (44.5%) individuals reported that they have no familial history of anxiety disorder diagnoses. 14 (11.8%) of individuals reported that familial history indicates anxiety disorder diagnoses between birth and 16 years of age. 37 (31.1%) of individuals reported that familial history indicates anxiety disorder diagnoses between 16 and 25 years of age. 12 (10.1%) of individuals reported that familial history indicates anxiety disorder diagnoses between 26 and 40 years of age. 3 (2.5%) of individuals reported that familial history indicates anxiety disorder diagnoses between 41 and 55 years of age. No familial histories had anxiety disorder diagnoses above the age of 56 years of age.

Familial Age When Immune System Disorder Diagnosis was Obtained

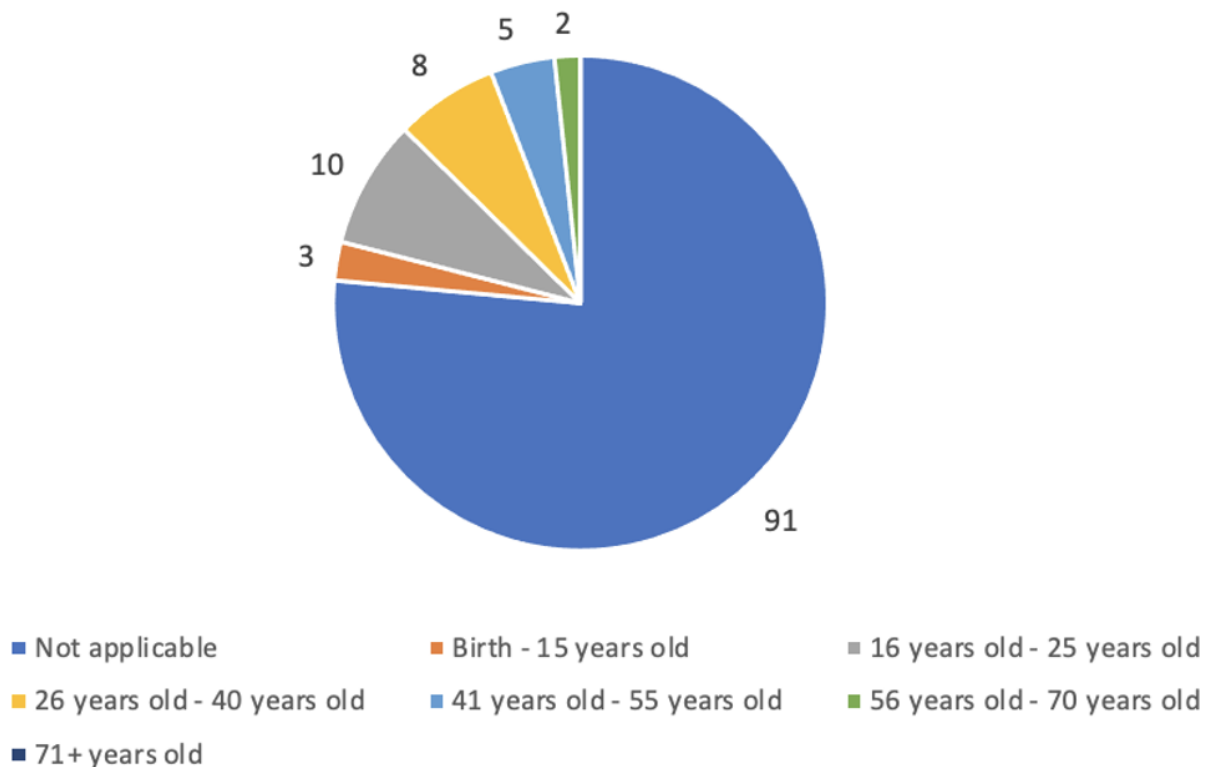


Figure 9. “If applicable, which age range best describes the age that you and your family history has obtained a diagnosis for immune system disorders?” 91 (76.5%) of individuals indicate that they have no familial history of immune system disorder diagnoses. 3 (2.5%) of individuals reported that familial history indicates immune system disorder diagnoses between birth and 15 years of age. 10 (8.4%) of individuals reported that familial history indicates immune system disorder diagnoses between 16 and 25 years of age. 8 (6.7%) of individuals reported that familial history indicates immune system disorder diagnoses between 26 and 40 years of age. 5 (4.2%) of individuals reported that familial history indicates immune system disorder diagnoses between 41 and 55 years of age. 2 (1.7%) of individuals reported that familial history indicates immune system disorder diagnoses between 56 and 70 years of age. No familial histories had immune system disorder diagnoses above the age of 71 years of age.

APPENDIX

SAMPLE SURVEY

1. What is your age?
2. Have you ever been diagnosed with an anxiety disorder by a certified medical professional?
 - a. Yes
 - b. No
3. If you answered yes to the previous questions, please specify which type of anxiety disorder you have been diagnosed with.
 - a. [Free response]
4. Have you ever been diagnosed with an immune system disorder by a certified medical professional?
 - a. Yes
 - b. No
5. If you answered yes to the previous question, please specify which type of immune system disorder that you have been diagnosed with.
 - a. [Free response]
6. Please select the statement listed below that most accurately describes you:
 - a. I have been diagnosed with one or more anxiety disorder(s), but not an immune system disorder
 - b. I have been diagnosed with one or more immune system disorder(s) by a medical professional
 - c. I have been diagnosed with one or more anxiety disorder(s) AND one or more immune system disorder(s)
 - d. I have not been diagnosed with an anxiety disorder OR an immune system disorder
7. If you indicated that you have been diagnosed with an anxiety disorder, do you currently or have you taken medication in order to aid in controlling your anxiety disorder symptoms? If applicable, do you feel that medication is beneficial to managing your anxiety?
 - a. Yes - Medication is beneficial
 - b. Yes - Medication is not beneficial
 - c. No
8. If you indicated that you have been diagnosed with an immune system disorder, do you currently take medication or have taken medication in the past in order to aid in controlling your immune system disorder symptoms? If applicable, do you feel that medication is beneficial to the management of your immune system disorder?
 - a. Yes - Medication is beneficial
 - b. Yes - Medication is not beneficial
 - c. No

9. Please select the statement that generally describes your family history, not including yourself:
- a. My family has a history of being diagnosed with one or more anxiety disorder(s), but not immune system disorders
 - b. My family has a history of being diagnosed with one or more immune system disorder(s), but not anxiety disorders
 - c. My family has a history of being diagnosed with both one of more anxiety disorder(s) AND one or more immune system disorder(s)
 - d. My family has no history of being diagnosed with neither anxiety disorders nor immune system disorders
10. If applicable, what age range best suits the age that you and your family have obtained a diagnosis for their anxiety disorder?
- a. Not applicable
 - b. Birth - 15 years old
 - c. 16 years old - 25 years old
 - d. 26 years old - 40 years old
 - e. 41 years old - 55 years old
 - f. 56 years old - 70 years old
 - g. 71+ years old
11. If applicable, what age range best describes the age that you and your family history have obtained a diagnosis for immune system disorders?
- a. Not applicable
 - b. Birth - 15 years old
 - c. 16 years old - 25 years old
 - d. 26 years old - 40 years old
 - e. 41 years old - 55 years old
 - f. 56 years old - 70 years old
 - g. 71+ years old

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