

The Relationship Between Inflammatory Bowel Diseases and Psychological Well-Being

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Abstract

Inflammatory Bowel Diseases (IBDs) are an incredibly crucial issue affecting society.

This paper focuses on the link between IBDs and mental health disorders such as anxiety, depression, and stress. This paper will review a series of studies concerning IBDs and other mental diseases and how they are related both empirically and mechanistically. Additionally, this paper will assess certain treatment methods that have some potential for treating IBDs such as mindfulness-based and acceptance-commitment approaches. This literature review is crucial for the continuation of research in the field of Inflammatory Bowel Disorders as well as the realm of mental health.

Keywords: Inflammatory Bowel Diseases, mental health disorders, treatment

Inflammatory Bowel Diseases (IBDs) are some of the more pressing issues plaguing medicine and society as a whole today. IBDs are categorized as inflammatory conditions of the colon and small intestine. The two principal and most well-known of these are Crohn's Disease and Ulcerative Colitis, whereas other conditions such as Microscopic Colitis, Diversion Colitis, and Behçet's Disease are less common. These diseases are often accompanied by a plethora of symptoms such as abdominal pain, bloody stool, rectal bleeding, weight loss, diarrhea, and fatigue. As it pertains to causes, scientists and medical professionals believe that an interplay of genetic predispositions and environmental factors are responsible, along with entropy in the gastrointestinal microbiome. According to the Center for Disease Control, In 2015, an estimated 1.3% of adults in the United States (around 3 million) were reported being diagnosed with an IBD (either Ulcerative Colitis or Crohn's Disease). This was a large increase from 1999 (0.9% or 2 million adults). These upticks in diagnoses in general are potentially due to a Western-style diet heavy in processed foods and a lack of anti-inflammatory ingredients found in areas with low rates of Inflammatory Bowel Diseases such as South East Asia and Africa. Although there exists many treatments currently available for IBDs and plenty of research initiatives on the causes and treatment methods of IBDs, the effects of these diseases on the patients themselves are equally important. Over the years, as Inflammatory Bowel Disorders have seen an increase in prevalence, patients suffering from these conditions expressed concerns over their mental states. This led to an increase in research as to how an IBD may affect a person's mental state, and vice versa, highlighting the relationship between the brain and the gastrointestinal system. These studies attempt to illustrate the link that patients diagnosed with an IBD are more likely to experience mental disorders such as anxiety and depression, environmental and biological factors

may cause an IBD, and that certain therapy treatments such as mindfulness-based and acceptance-commitment approaches may be critical in mitigating and treating the harmful mental aspects of these diseases. This paper will examine both the empirical and mechanistic evidence for an increased risk of mental illness in relation to Inflammatory Bowel Diseases as well as potential treatment methods for these mental illnesses in a literature review.

Mechanistic Evidence

There are certain important factors to consider when evaluating any potential link between Inflammatory Bowel Diseases and mental conditions such as anxiety and depression. One of these factors includes mechanistic evidence. Various studies have taken steps in order to ascertain that information as it pertains to the link between IBDs and mental health disorders. Abautret-Daly, Dempsey, Parra-Blanco, Medina, and Harkin conducted a study in 2018 where they examined the likely mechanics linking the gastrointestinal system to the brain itself. They reviewed the evidence that supports that inflammation as a whole plays a key role in the pathophysiology of mood disorders such as schizophrenia, major depressive disorder, and bipolar disorder (Abautret-Daly et al., 2018). Patients suffering from all of these conditions have been shown to have elevated levels of pro-inflammatory cytokines (Abautret-Daly et al., 2018). According to the study, both clinical and preclinical cases have shown that otherwise healthy patients display “poor mood and ‘sickness behaviour’; a behavioural phenotype resembling depression with symptoms including lethargy, anxiety, social withdrawal, anhedonia and anorexia” when induced into a pro-inflammatory state (Abautret-Daly et al., 2018). The study also analyzed animal models used to ascertain the connection between gastrointestinal disruption

and certain psychological manifestations. These included numerous infection models by bacteria which “colonise and disrupt tissue in the GI tract of mice and are effective models of acute colitis” such as *Citrobacter rodentium* and *Campylobacter jejuni* (Abautret-Daly et al., 2018). Furthermore, according to Abautret-Daly et al., there exists a bidirectional connection known as the “gut–brain axis” which consists of hormonal, neural, and immune communication links. This link includes a number of interacting factors such as the activation of the inflammatory response system in the brain which affects the hypothalamic-pituitary-adrenal axis, changes in blood brain barrier integrity, as well as a disruption in gut microbiota in response to Inflammatory Bowel Disorders (Abautret-Daly et al., 2018). Clearly, there exists a connection between the gastrointestinal system and the brain which is activated during exposure to inflammation.

A study conducted by Alhouayek, Lambert, Delzenne, Cani, and Muccioli in 2011 analyzed the mechanistic evidence in the role of inflammation and brain functioning in patients with chronic bowel diseases. Previous research, along with genetic and pharmacological data, point to a relatively protective role of the CB₁ and CB₂ cannabinoid receptor activation in IBD experimental models of past studies. According to Alhouayek et al., the logical next step would be to increase the endogenous levels of 2-arachidonoylglycerol, the primary total agonist of these receptors, which should induce beneficial effects on patients with Inflammatory Bowel Diseases (Alhouayek et al., 2011). Using mouse models, arachidonoylglycerol levels were elevated in the trinitrobenzene sulfonic acid (TNBS)-induced colitis mice via inhibition of monoacylglycerol lipase (MAGL), the main enzyme responsible for the hydrolysis of 2-arachidonoylglycerol, using the selective inhibitor “JZL184” (Alhouayek et al., 2011). The researchers found that MAGL inhibition in mice with colitis increased 2-arachidonoylglycerol

levels, leading to a decrease of histological and microscopic colon changes, as well as a reduction of the colonic expression of pro-inflammatory cytokines (Alhouayek et al., 2011). As a result, the restored integrity of the gastrointestinal barrier functioning after the MAGL inhibition led to decreased endotoxemia as well as reduced brain and peripheral inflammation. (Alhouayek et al., 2011). Ultimately, the experiment also showed that co-administration of either the CB₁ (SR141716A) or CB₂ (AM630) selective antagonists with JZL184 completely nullified the protection effect of the MAGL inhibition on the TNBS-induced colon alterations, thereby demonstrating the clear involvement of both cannabinoid receptors in chronic inflammation and inflammatory bowel diseases (Alhouayek et al., 2011). The researchers believe that the results of this study could be beneficial since peripheral inflammation is often coupled with CNS inflammation, which triggers behavioral and pathological alterations such as depression, sickness behavior, and enhanced susceptibility to seizures (Alhouayek et al., 2011). Being able to control this inflammation and the receptors may prove critical to treating the mental health conditions of patients with IBDs.

Bonaz and Bernstein performed a study in 2013 where they examined Psycho-neuro-endocrine-immune modulation via the brain-gut axis. The researchers believe that this likely plays a key role in the pathogenesis of inflammatory bowel diseases (Bonaz and Bernstein, 2013). The brain-gut axis includes numerous interactions among several neural components, such as the central nervous system, the autonomic nervous system, the (gastrointestinal) corticotropin-releasing factor system, the stress system (hypothalamic-pituitary-adrenal axis), and the intestinal response (including the intestinal barrier, the luminal microbiota, and the intestinal immune response) (Bonaz and Bernstein, 2013).

According to animal models, the intestinal microbiota can act as a mediator in communication between the gut and the brain, also known as the microbiota brain-gut axis. Laboratory mice treated with *Campylobacter jejuni* showed vagally mediated activation in the Nucleus Tractus Solitarius (NTS), the area of the brainstem critical to immune-to-brain signaling, in the absence of intestinal inflammation (Bonaz and Bernstein, 2013). The models also found that commensal microbiota can alter the postnatal development of various brain systems involved in the endocrine response to stress (Bonaz and Bernstein, 2013). Furthermore, they found that exposure of mice to a social stressor affected the structure of intestinal microbiota and increased the circulating level of cytokines. Additionally, changes in the intestinal microbiota were found to reduce overall resistance to infectious challenges with pathogens in the intestine. These revelations provide data and evidence for the interconnection between stress, the intestinal microbiota, and the eventual immune response (Bonaz and Bernstein, 2013). The researchers believe that physicians and clinicians need to address these critical issues among patients due to emerging evidence that stress or other harmful psychological conditions may have an adverse effect on the course of the disease itself. Given that inflammation can trigger psychological problems on its own, the fact that it can become a cycle of inflammation causing stress, which in turn causes more immune responses and inflammation, should worry the scientific community and inspire more research to be conducted to address this critical issue in gut-brain health.

In a study conducted in 2016 by Martin-Subero, Anderson, Kanchanatawan, and Berk, the researchers evaluated the comorbidity between inflammatory bowel diseases and depression by analyzing the pathways in the gut-brain system. In researching the link between depression and inflammation, they found, in cases of IBDs, elevated levels of pro-inflammatory cytokines

(PICs), including IL-1, IL-6, IL-8, IL-12, and the tumor necrosis factor-alpha (TNF α) coupled to decreased levels of anti-inflammatory cytokines, such as transforming growth factor-beta (TGF- β) and IL-10 (Martin-Subero et al., 2016). These findings are significant because the levels of IL-6R are significantly elevated in cases of unipolar depression and bipolar disorder, which suggests that these diseases are accompanied by increased IL-6 trans-signaling. Increased IL-6 trans-signaling is considered by researchers to be critical to analyzing the pathophysiology of depression (Martin-Subero et al., 2016). Furthermore, increased IL-1R antagonist (IL-1RA) levels in cases of depression further emphasizes inflammatory processes in depression (Martin-Subero et al., 2016). Additionally, the researchers found increased oxidative and nitrosative stress levels (O&NS) with damage to lipids, proteins, and DNA (Martin-Subero et al., 2016). These findings are critical since heightened immune-inflammatory, oxidative, and nitrosative stress (IO&NS) pathway processes in cases of depression tend to overlap with the biological groundwork of inflammatory bowel disorders, which could potentially explain the increased frequency of their co-occurrence. Clearly, various pathways related to stress have connections to the inflammatory tracts, which may play a role in inflammation and its relation to psychological illnesses.

A study conducted by Stasi and Orlandelli in 2008 aimed to analyze the role of the brain-gut axis in the pathophysiology of Crohn's disease. They focused on the interactions between the gastrointestinal system and the central nervous system since it has shed light on the neurobiological responses to stress by means of the hypothalamic-pituitary-adrenal axis (HPA) and the hypothalamic-autonomic nervous system axis (Stasi and Orlandelli, 2008). Researchers found that in numerous chronic diseases and stress-related psychological disorders, an alteration

has been observed of the HPA response. This response is important because it modulates through glucocorticoids the immuno-inflammatory reactions (Stasi and Orlandelli, 2008). In the study, it was found that in animal models of colitis, environmental and/or psychological stress may increase permeability of the gastrointestinal tract. This in turn results in abnormal antigen activity with respect to the immune system and ultimately leads to the perpetuation and exacerbation of inflammation in the intestinal pathways (Stasi and Orlandelli, 2008). The researchers discovered that increased intestinal permeability as a result of stress is mediated through nicotinic, adrenergic and cholinergic receptors by corticotropin-releasing hormone stimulation (Stasi and Orlandelli, 2008). These revelations suggest a complex relationship between both the parasympathetic and sympathetic nervous systems which could prove useful for future research. By focusing on Crohn's Disease, which is noted for having its patients experiencing a higher prevalence of psychiatric diagnoses, the researchers provide critical information that can lead to the amelioration of suffering in Crohn's patients as well as in the generic sphere of patients battling inflammatory bowel diseases.

Gastrointestinal permeability remains a common issue when analyzing the mechanistic evidence for a link between inflammatory bowel diseases and psychological well being. In a study performed in 2000, Meddings and Swain evaluated environmental stress-induced gastrointestinal permeability in laboratory rat models. The researchers first examined a candidate theory for the cause of Crohn's Disease, being an abnormal presentation of luminal constituents to the mucosal immune system, which is ultimately caused by dysfunction of the intestinal epithelial barrier (Meddings and Swain, 2000). According to previous studies, increased epithelial permeability can be found in certain subgroups of patients at high risk for development

of Crohn's disease and has sometimes been found to precede the disease's recurrence (Meddings and Swain, 2000). Certain clinical observations have implied that disease recurrence can follow periods of elevated psychological stress, which led the researchers to hypothesize that environmental stress would increase gastrointestinal permeability (Meddings and Swain, 2000). Using laboratory rat models, the researchers found that increased epithelial permeability, after increasing stress in rats, was observed in all regions of the gastrointestinal tract and appeared to be mediated by adrenal corticosteroids (Meddings and Swain, 2000). In the study, dexamethasone treatment of the control rats increased gastrointestinal permeability and mimicked the effects of stress. Additionally, the stress-induced augmentations in epithelial permeability vanished after an adrenalectomy or a pharmacologic blockage of glucocorticoid receptors. This study confirms that there exists a complicated relationship between IBDs and stress, and that link can function via numerous pathways and venues as opposed to a single, concrete source.

Empirical Evidence

A study conducted by Addolorato, Capristo, Stefanini, and Gasbarrini in 1997 examined the association between depression, anxiety, nutritional status, physical morbidity, and inflammatory bowel diseases. This study was designed to highlight cases of anxiety and depression in subjects affected by various inflammatory bowel diseases and to determine the influence and role of physical morbidity and nutritional status on certain psychological illnesses (Addolorato et al., 1997). The researchers utilized 79 patients, 36 with ulcerative colitis and 43 with Crohn's disease in their study. In order to evaluate each patient, the researchers obtained an

index of disease activity and the patient's physical morbidity utilizing the simplified Crohn's Disease Activity Index and Truelove-Witts criteria, while also using the Clinical Rating Scale (Addolorato et al., 1997). In order to account for a control population, 36 healthy volunteers were also studied. As part of the study, all of the participants were given the Zung self-rating Depression Scale and the State and Trait Anxiety Inventory (STAI) test (Addolorato et al., 1997). Through their study, the researchers found that the percentage of subjects categorized with anxiety was significantly higher in the Crohn's disease ($P < 0.001$) and ulcerative colitis ($P < 0.001$) groups than in the control participants (Addolorato et al., 1997). The percentage of subjects categorized with depression ended up significantly higher in the Crohn's disease ($P < 0.05$) and ulcerative colitis ($P < 0.05$) groups than in the control participants (Addolorato et al., 1997). Additionally, anxiety and depression in the subjects were significantly correlated with patient physical morbidity and malnutrition in both the Crohn's disease and ulcerative colitis patients (Addolorato et al., 1997). This study highlights the importance of evaluating the psychological aspect of inflammatory bowel diseases, given that there was a significant correlation for patients experiencing depression as well as physical morbidity and malnutrition.

Burke, Meyer, Kocoshis, Orenstein, Chandra, Nord, Sauer, and Cohen performed a study in 1989 where they analyzed anxiety and depression in pediatric cases of inflammatory bowel diseases and cystic fibrosis. In the study, they evaluated 52 children with cystic fibrosis, 41 children with Crohn's disease, and 12 children with ulcerative colitis, utilizing the Kiddie-Schedule for Affective Disorders and Schizophrenia evaluation (Burket et al., 1989). The researchers found that the lifetime prevalence of depression was 21% in ulcerative colitis, 29% in Crohn's disease, and 11.5% in cystic fibrosis (Burke et al., 1989). They also discovered that

the difference in the prevalence of depression between Crohn's disease and cystic fibrosis was significant (p less than 0.05). The lifetime and current prevalence of dysthymia, a type of depression, was significantly greater in ulcerative colitis patients than cystic fibrosis patients (p less than 0.01) or Crohn's disease patients (p less than 0.01) (Burke et al., 1989). The researchers also found that lifetime prevalence of atypical depression was significantly larger in Crohn's disease patients than cystic fibrosis (22% versus 5.8%, p less than 0.05) and was also greater in patients with ulcerative colitis compared to those with cystic fibrosis (21% versus 5.8%, $p = 0.1$) (Burke et al., 1989). This study indicates that mental health issues are not only found in adult populations of patients with inflammatory bowel disorders, but they can also be found in pediatric patients. This information can be relevant in future treatment and diagnosis of these diseases.

In 2017 Chan, Shim, Lim, Sawadjaan, Isaac, Chuah, Leong, and Kong conducted a study where they aimed to assess the relationship between symptoms of depression and anxiety, disability, and quality of life in a population of Singaporean patients with inflammatory bowel diseases. The researchers conducted a cross-sectional study where they utilized the Hospital Anxiety and Depression Scale (HADS), IBD questionnaire (IBDQ), and IBD-Disability Index (IBD-DI) (Chan et al., 2017). They recruited 200 consecutive subjects, (males: 69%; median age: 43.8 (\pm 15.4) years; of which 105 had ulcerative colitis (UC) and 95 had Crohn's disease (CD); median IBD duration: 10.8 (\pm 9.0) years.) (Chan et al., 2017). A total of 27% of the subject cohort were ultimately recorded as having anxiety and/or depression, which eventually worsened their disability. The IBD-DI recorded a score of -9 (\pm 14) with anxiety vs 6 (\pm 13) without anxiety, $P < 0.001$; whereas for depression the score was -12 (\pm 16) as opposed to 5 (\pm 13)

without depression, $P < 0.001$) (Chan et al., 2017). Clearly, symptoms of depression and anxiety were common in this group of IBD patients and these symptoms were greatly associated with worsening of their IBD condition. By recognizing these psychological issues contributing to overall disability in IBD patients remains critical to guarantee the appropriate treatment and holistic care for each patient.

A study conducted by Engström in 1999 studied the psychological effect of inflammatory bowel diseases in pediatric and adolescent patients. The researchers utilized a design comprising both semi-quantitative self-reporting measures, such as questionnaires and rating scales, as well as utilizing comprehensive interviews with both the child and their parents. Additionally, the study also examined matched children with diabetes and chronic tension headaches and matched children without chronic physical disease as clinical comparison groups (Engström, 1999). The study consisted of 80 subjects, with an age range of 9 to 18. In the group of IBD patients, there were 9 with Crohn's disease and 11 subjects with ulcerative colitis (Engström, 1999). According to the researchers, the study showed that inflammatory bowel diseases often lead to psychiatric complications. Among the patients, it was common to see certain emotional disorders, such as depression and anxiety symptoms (Engström, 1999). Utilizing the Child Assessment Schedule interview, the results revealed a prevalence of psychiatric disorders in approximately 60% of patients in the IBD group. Of these 60%, half were considered to be moderate or severe disorders that disrupted the patient's daily routine (Engström, 1999). This study depicts that the well-being of a chronically ill pediatric patient rests not only on the set course of the chronic disease and its physical symptoms but also on the social and psychological detriments that seem to run concurrently with this type of a disease. Clearly, the importance of monitoring and addressing

aspects of the psychosocial impact of inflammatory bowel diseases on patients is paramount to their wellbeing and recovery.

Kao, Lin, and Lee performed a study in 2019 where they aimed to evaluate the link between inflammatory bowel diseases (IBDs) and bipolar disorder (BD). Utilizing Taiwan's National Health Insurance Research Database, the researchers evaluated 3590 patients with IBDs and 14,360 comparison patients without an IBD in this study (Kao et al., 2019). The study showed that bipolar disorder was found in 26 (0.72%) patients with an inflammatory bowel disease and in 49 (0.34%) comparison patients without an inflammatory bowel disease (Kao et al., 2019). However, after adjustment, the adjusted odds-ratio of bipolar disorder for IBD patients was 2.10 (95% confidence interval (CI): 1.30~3.38) compared to the other group (Kao et al., 2019). Additionally, this study depicted that the adjusted odds-ratio of BD for patients diagnosed with ulcerative colitis (UC) were 2.23 (95% CI: 1.31~3.82) as compared to the other group (Kao et al., 2019). Clearly, patients with an inflammatory bowel disease were more likely to experience bipolar disorder. This study's findings are crucial due to the fact that the psychological illnesses patients with inflammatory bowel disorders experience are not just limited to anxiety and depression, but they also include disorders such as BD. This could be useful in the future treatment of IBDs since physicians would know that the parameters for experienced psychological issues are broader than previously thought.

In 2011, Loftus et al. conducted a study analyzing Crohn's disease (CD) and its connection to psychological well-being. Given that IBDs such as CD are often associated with critical psychosocial burdens and elevated risks for mental health conditions, the researchers analyzed the risks of developing depression and anxiety as well as accounts of psychotropic

medication usage between a population of young CD patients and their matched controls without Crohn's disease. The researchers gathered information from the MarketScan database, with five non-CD patients matched per each CD patient (Loftus et al., 2011). After analyzing risks and incidence rates of developing anxiety disorders and depression, as well as psychotropic medication usage in the 6 months following the index date, the study found that the rates of developing depression ([95% Confidence Interval] =1.74 [1.35–2.25]) and anxiety ([95% Confidence Interval] =2.28 [1.65–3.17]) among patients were significantly higher for the Crohn's disease cohort ($N=2,144$) as opposed to the non-CD control patients ($N=10,720$) (Loftus et al., 2011). Patients with Crohn's disease were also reported to have elevated risks of developing persistent anxiety and depression ([95% Confidence Interval] =4.35 [2.22–8.50] and 2.75 [1.73–4.38], respectively) (Loftus et al., 2011). Given that these patients were young, all less than 18 years of age, these results are critical to shedding light on pediatric IBD cases and their complications, both relating to physical and mental health.

A study conducted by Piacentino et al. in 2019 aimed to evaluate the overall role of psychopathology in cases of inflammatory bowel diseases (IBDs) and irritable bowel syndrome (IBS). In order to understand this role, the researchers compared the psychopathological features of IBD and IBS in both healthy and sick patients while also evaluating any potential correlation between presence of psychopathological features and disease severity in sick patients. The study utilized 69 patients with IBDs, of which 35 had ulcerative colitis and 34 had Crohn's disease (Piacentino et al., 2019). Additionally, the study utilized 75 patients with IBS and 76 healthy control patients. The patients' psychological state was evaluated utilizing the Symptom Checklist-90-Revised (SCL-90-R) (Piacentino et al., 2019). According to the study, the IBD and

IBS patients displayed significantly greater scores on the SCL-90-R Global Severity Index (GSI) and its subscales compared to the non-IBS/IBD controls (all p -values <0.001), and IBS patients displayed significantly greater GSI, depression, and anxiety scores (all p -values <0.01) (Piacentino et al., 2019). Additionally, the researchers found that In IBD and IBS patients, the SCL-90-R GSI was significantly correlated with the disease's overall severity ($p<0.001$) (Piacentino et al., 2019). Ultimately, the existence of chronic bowel symptoms was linked to a significantly higher severity of a patient's psychopathology as compared to the general population. The researchers believe that this is possibly due to greater amounts of stress on the patient from the symptoms of IBD/IBS impacting their everyday life (Piacentino et al., 2019). Furthermore, the researchers found that in both IBS and IBD patients, higher disease severity and worse mental functioning were related (Piacentino et al., 2019). This study highlights the impact of gastrointestinal problems on a person's psychological state and how their symptoms can greatly impact a diagnosed individual's everyday life.

Romasenko, Makhov, and Isaykina performed a study in 2019 where they examined anxiety-depressive disorders among groups of patients with inflammatory bowel diseases in order to analyze any potential clinically important psychosomatic associations. As part of the study, the researchers examined and then later followed up with 50 patients with inflammatory bowel diseases, which consisted of 32 patients with ulcerative colitis and 19 patients with Crohn's disease. As a result, some form of depression was discovered in 72% of IBD cases (Romanesko et al., 2019). Additionally, cases of bipolar disorder, schizophrenia, and cyclothymia were identified among the patients as well. Furthermore, the researchers found that there were manifestations of depression consisting of different types with various durations

(bipolar, attack-like, recurrent) at the latter stages of IBDs (Romanesko et al., 2019). These findings are significant because they illustrate the myriad of psychological conditions a patient with an inflammatory bowel disease may encounter and because they depict that as the duration of the disease progresses, there are manifestations of these psychological conditions. This will be of value for studies that are pursuing a longitudinal approach and want to evaluate the best long-term treatment for IBDs.

In 2019, Thakur et al. conducted a study analyzing the prevalence and incidence of various psychological conditions such as depression, post-traumatic stress disorder (PTSD), and anxiety in a group of United States veterans with inflammatory bowel diseases (IBDs). The researchers evaluated the presence of depression, PTSD, and anxiety among a group of veterans with Crohn's disease or ulcerative colitis throughout fiscal years 2000-2015. The study made sure to exclude patients with prior depression, PTSD, or anxiety prior to their first Veterans Health Administration IBD encounter from the patient group in order to ensure the most accurate representative group of patients (Thakur et al., 2019). The researchers calculated the incidence rates, annual prevalence, and stratified the patients by gender as well as standardized by age utilizing a direct standardization method (Thakur et al., 2019). The study involved a total of 60,086 IBD patients, of which 93.9% male. The researchers found that the prevalence of depression, PTSD, and anxiety grew from 10.8 per 100 with an IBD in 2001 to 38 per 100 with an IBD in 2015 (Thakur et al., 2019). As a result, a total of 19,595 (32.6%) of the patients received a new depression, PTSD, and/or anxiety diagnosis during the overall study period (Thakur et al., 2019). Conclusively, the presence of depression, PTSD, and/or anxiety was relatively high among US veterans with inflammatory bowel diseases, consisting of a third of the

patient group, and increasing, given the chronic duration of IBDs and various psychological illnesses. This study was critical due to the fact that veterans as a whole are not studied as often as the general population, especially in the field of gastrointestinal illnesses.

A study conducted by Thavamani, Umapathi, Khatana, and Gulati in 2019 aimed to ascertain the burden of psychological conditions among a group of pediatric and young adults diagnosed with inflammatory bowel diseases. The researchers performed a retrospective case control analysis utilizing a database which included sets of data spanning across a total of 26 health care networks, which comprised over 360 hospitals across the United States. The data collected from these various hospitals were stored and organized according to Systematized Nomenclature of Medicine-Clinical Terms (Thavamani et al., 2019). According to the study, the researchers pre-identified a total of 10 psychiatric disorders and then examined the database for the existence of at least one of those 10 selected psychiatric disorders among patients with an IBD between ages ranging from 5 and 24 years old (Thavamani et al., 2019). These patients were later compared to the controls. A total of 11,316,450 patients were analyzed in the age parameter ranging from 5 and 24 years old, with the total count of patients diagnosed with an IBD, either Crohn's disease or ulcerative colitis, being 58,020 (Thavamani et al., 2019). The researchers found that the prevalence of psychiatric conditions was 21.6% among the IBD patient group, comprising mostly of depression and anxiety disorders (Thavamani et al., 2019). Following various logistic regression analyses, the results showed that patients with an IBD were 5 times more likely to experience psychiatric disorders compared to the control group ($p < 0.001$) (Thavamani et al., 2019). Additionally, the study's analysis depicted a steady increase in the prevalence of psychiatric conditions among IBD patients, from 2% in 2006 to 15% in 2017

(Thavamani et al., 2019). This study is critical because it highlights the fact that the psychological disorders experienced by patients with IBDs are not limited to only depression or anxiety, instead they can have a broad range of diagnoses.

Yongwen et al. performed a study in 2018 where they compared the prevalence of anxiety and depression among patients diagnosed with complex and uncomplicated inflammatory bowel diseases (IBDs). The study involved a set of uncomplicated and complex IBD patients that were evaluated using the Hospital Anxiety and Depression Scale (HADS) and the Short Form-12 (SF-12), a demographic questionnaire (Yongwen et al., 2018). In regards to terminology, the complex IBD patients were categorized as those specifically dealing with active inflammation, surgical, and/or nutritional issues. As it pertained to all other IBD patients, they were identified as those with an uncomplicated case of IBD. Following a review of the SF-12 scores, the results depicted that scores in the Physical Component Summary were below average in 56.0% and 71.9% of the uncomplicated and complex patients, respectively ($p < .001$) (Yongwen et al., 2018). Furthermore, the scores for the Mental Component Summary were below average in 45.3% and 65.6% of the uncomplicated and complex patients, respectively ($p < .001$) (Yongwen et al., 2018). Additionally, HADS scores in the uncomplicated and complex IBD patients showed that 18.5% and 29.2%, respectively, were cases of anxiety ($p < .1$) and that 15.9% and 32.3%, respectively, were cases of depression ($p < .001$) (Yongwen et al., 2018). Clearly, having a severe case of an inflammatory bowel disease was linked to a greater prevalence of psychological issues such as anxiety and depression. This study highlights the importance of understanding what how the severity of an IBD may affect a patient.

Potential Treatment Methods

Although the mechanistic and empirical evidence for a link between inflammatory bowel diseases and the mental illnesses that accompany them is crucial, the path forward in terms of potential treatment for those mental illnesses must also be evaluated. In a study conducted by Gracie et al. in 2017, the researchers analyzed the effect of psychological therapy on the quality of life, disease activity, and psychological comorbidity in a review of studies involving IBD patients. By means of a systematic trial review, the researchers identified numerous randomised controlled trials (RCTs) that recruited groups of patients aged 16 years or older with IBDs which compared a usual treatment or control intervention with psychological therapy. In doing so, they identified 1824 studies, with 1196 patients from 14 RCTs able to be included (Gracie et al., 2017). The analysis depicted a significant difference in scores for quality of life ($p=0.01$) and depression ($p=0.04$) with the utilization of psychological therapy versus the control sample (Gracie et al., 2017). The researchers also evaluated the effect of individual physiological therapies on the patient's quality of life. They found that only cognitive behavioural therapy (CBT) had any relevant or significant beneficial effect on the patient's condition (Gracie et al., 2017). This study and others like it are relevant because they demonstrate that an IBD patient's condition can be ameliorated when undergoing therapy for the psychological conditions they may be facing as a result of their illness.

A study conducted by Shoultz, Atherton, and Watson in 2015 analyzed the efficacy of mindfulness-based cognitive therapy for patients with an inflammatory bowel disease. Mindfulness-based Cognitive Therapy (MBCT) can be described as an evidence-based psychological method formulated to help control symptoms of stress and depression. According

to the researchers, there have been no randomized controlled trials (RCT) examining the utilization of MBCT in patients with an IBD. The patients with an IBD were recruited from several gastroenterology outpatient clinics from two Scottish NHS Boards and were randomly divided into a wait-list control group (n = 22) or a MBCT intervention group (n = 22) (Shoultz et al., 2015). Overall, the MBCT intervention consisted of a total of 16 hours of organized group instruction over a period of 8 consecutive weeks in addition to instructed home practice and further follow-up therapy sessions (Shoultz et al., 2015). All of the patients filled out an initial, post-therapy, and follow up assessment six months later (Shoultz et al., 2015). The researchers found that when analyzed at the post-intervention and follow-up, the patients in the MBCT group showed a significant improvement of scores for trait anxiety, dispositional mindfulness, and depression when compared to the control group (Shoultz et al., 2015). This study shows that MBCT could be an option when treating the psychological problems associated with IBDs.

Wynne et al. performed a study in 2019 where they evaluated how efficient acceptance and commitment therapy (ACT) can be at reducing stress in inflammatory bowel disease (IBD) patients. The researchers performed a randomized controlled trial with a total of 122 patients with manageable or mildly active IBDs that were randomly allocated to an 8-week ACT treatment and the control group followed treatment protocol as usual (Wynne et al., 2019). At the baseline, eight week mark, and three months post-intervention (week 20), the researchers collected demographic, clinical, psychological, and disease activity data, as well as feces and blood samples (Wynne et al., 2019). Additionally, they collected scalp hair from the patients at the baseline and at week 20 in order to measure concentrations of steroids (Wynne et al., 2019). In the study, the primary endpoint was the difference in stress symptoms, which was evaluated

with the Depression Anxiety Stress Scale (DASS). The secondary endpoints consisted of differences in anxiety, perceived stress, depression, disease activity, quality-of-life, and the concentration of cortisol in their hair (Wynne et al., 2019). According to the researchers, they found that there were 39% and 45% reductions in reported stress from baseline to 8 and 20 weeks respectively within the treatment group, compared to 8% and 11% reductions in the control group ($P = .001$) (Wynne et al., 2019). Additionally, ACT was linked to a reduction in depression ($P = .010$) and perceived stress ($P = .036$) compared with control individuals (Wynne et al., 2019). After analysis, the overall quality of life and well being improved in the ACT group compared to the non-ACT control group ($P = .009$) (Wynne et al., 2019). This study shows that therapy methods such as ACT can be critical in mitigating the harmful mental problems that often accompany IBDs.

Ultimately, Inflammatory Bowel Diseases (IBDs) are clearly an issue plaguing society as a whole. With hundreds of thousands of people living with these diseases in the United States alone and with the number of those diagnosed per year increasing, finding proper treatment for IBDs remains a necessity. Although there are a plethora of medications that can address IBD symptoms that patients suffer from, more research is required in order to address the psychological conditions patients may experience as a result of having an IBD in order to ameliorate their psychological wellbeing. As the studies this paper reviewed have indicated, there clearly exists a mechanistic link between the gastrointestinal system and the brain. Furthermore, according to the empirical evidence reviewed in this literature review, a statistically significant amount of patients with an IBD report some form of psychological problems, ranging

from depression, anxiety, bipolar disorder, etc. Despite these unfortunate statistics, there exists a light at the end of this tunnel. Several new studies have shown that specific types of therapy may be helpful in mitigating the mental toll an IBD may have on a patient. Unfortunately, there are few of these studies in existence and more research is definitely required and encouraged on that front. By combining regular IBD treatment protocol with potential therapy methods, physicians treating patients with IBDs can cover all bases in their treatment and make sure that they receive the quality of care they truly deserve. As this field of research broadens, patients with an IBD can finally address problems that often go unnoticed and live an improved life as a result.

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