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Research Article

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Psychopathological Characteristics in Patients with Digestive Problems: A Comparative Analysis with a Healthy Control Group

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Abstract

Introduction: *This study aimed to compare the psychopathological characteristics of patients with digestive (gastrointestinal) problems with those of a healthy control group.*

Methods: *A total of 70 patients with gastrointestinal issues were referred to the gastroenterology department, and 70 healthy individuals were included in the study. Both groups completed the 90-question mental health questionnaire (SCL-90-R).*

Results: *The results demonstrated significantly higher average scores in the patients' group across various scales, including depression, aggression, somatization, sensitivity in social relationships, obsession, anxiety, phobia, and psychotic symptoms. Overall, the group with digestive problems exhibited more symptoms associated with these eight mental disorders than the healthy control group. However, there were no notable differences between the two groups, except for the presence of paranoid ideations as a distinguishing characteristic.*

Conclusions: *This research unequivocally establishes a strong association between gastrointestinal issues and mental well-being, highlighting the influence of digestive system functioning on mental health. These findings contribute to a deeper understanding of the psychopathological aspects related to gastrointestinal conditions.*

Keywords: Digestive (Gastrointestinal) Problems, Mental Health, Psychopathological Characteristics.

1. Introduction

The human gastrointestinal (GI) system is home to symbiotic bacteria that serve as a piece of vital metabolic machinery [1]. Experts firmly hold the belief that the gut microbiome wields substantial influence over numerous physiological aspects, working its magic through intricate neural, hormonal, and immunological pathways [2]. Notably, the expansive composition of the gut microbiome, boasting around 1800 phyla and a staggering 40,000 bacterial species, has further solidified its involvement in these processes [3].

The bidirectional communication between the central nervous system and the gut microbiota is aptly referred to as the microbiota-gut-brain axis [4,5]. This intricate connection involves the transmission of signals and the modulation of central processes directly linked to the brain, including neurotransmission, neuroinflammation, and behavior. The Vagus nerve, in particular, is believed to play a significant role in this axis, further emphasizing its influence on the interconnected workings of the microbiota, gut, and brain [6,7].

The gut bacteria generate a diverse array of neuroactive substances, including catecholamines, histamine, and more. These substances have the potential to interact directly with receptors in the gastrointestinal tract or traverse the gut wall and enter the portal circulation through absorption or passive diffusion [8].

As a result, certain bacteria engage in the release of chemical factors, giving rise to a diverse array of physiologically active substances, including neuromodulators and neurotransmitters.

In addition, these substances have the potential to influence various gut activities, such as motility.9 Recent research has revealed that the normal intestinal microbiota plays a crucial role in regulating cerebral metabolites via the microbiota-gut-brain axis. This highlights the significance of the intestinal microbiota in maintaining brain health, impacting illness, development, attenuation, learning, memory, and behavior [7].

Furthermore, there is a growing proposition that gut bacteria could hold significant implications in the development and progression of numerous diseases, including mental illnesses, through the disruption of homeostasis [10]. Traditionally, mental disorders were primarily viewed as afflictions of the brain, with limited consideration given to the involvement of the body or individual organs. However, in line with modern psychosomatic medicine, it is now recognized that factors such as stress, emotions, and cognitive processes can profoundly impact bodily functions. In addition, clinical observations, based on anecdotal evidence, among individuals affected by anxiety, depression, and autism spectrum disorder (ASD) suggest that altered signaling between the gut and the brain may play a pivotal role. Notably, many of these studies have focused on psychiatric conditions as co-existing with gut disorders, with the latter often identified as the primary diagnosis [11].

Intestinal epithelial barriers comprise roughly 70% of the immune system, highlighting their pivotal role [12]. Immune responses, particularly those involving the epithelial barrier, are crucial for maintaining immune system balance and curbing inflammatory reactions [13]. The impact of the gut microbial population on the immune system's function, maintenance, and development is of great significance. This influence stems from the continuous exposure of the body to antigens and immunomodulatory components delivered through food and commensal microbiota. This interaction leads to various effects, such as the increased expression of antimicrobial peptides by intestinal epithelial cells, the regeneration of islet-derived protein, the increased expression of IgA-producing B cells, the promotion of antibody and cytokine production, and the induction of T cell differentiation. These factors collectively shape immunity by influencing the maturation of gut-associated lymphoid tissue and innate lymphoid cells [14].

The establishment of the gut microbiota commences during infancy, and by the age of three, the microbial composition of newborns closely resembles that of adults. While the gut microbiota typically remains stable in adults, lifestyle factors can disrupt this equilibrium, leading to a state of dysbiosis [15,16].

Dysbiosis refers to any alteration in the symbiotic microbial community residing in the human gut, deviating from the composition observed in a healthy population. This shift can be triggered by various factors, including dietary choices, certain medications, and exposure to toxins and pathogens [17,18]. The consequences of gut dysbiosis are far-reaching, as it has been associated with inflammatory conditions such as inflammatory bowel disease, allergies, asthma, obesity, metabolic syndrome, type 1 and type 2 diabetes, and central nervous system (CNS) disorders [19].

Within our peripheral nervous system exists a highly innervated neural network known as the enteric nervous system (ENS), often called our "second brain." This intricate network facilitates communication between the central nervous system (CNS) and the gastrointestinal (GI) tract. While mental disorders have traditionally been viewed as diseases primarily affecting the CNS, they are fundamentally neurological. Notably, anxiety disorders frequently co-occur with functional GI disorders and gut symptoms are commonly observed somatic symptoms associated with depression. Furthermore, irritable bowel syndrome (IBS) has shown a positive response to treatment with antidepressants and psychological therapies, thus underscoring the systemic nature of mental disorders rather than solely CNS-related disorders [20].

Multiple surveys consistently show that people with mental disorders, such as depression, psychosis, and bipolar disorder, have dissimilar gut microbiota composition compared to control subjects [20].

Preclinical studies have provided insights into the impact of gastrointestinal (GI) microbiota on mental disorders. Researchers have demonstrated that germ-free mice exhibit heightened physiological responses to stress compared to mice with pathogen-free microbiota. Moreover, the introduction of reconstituted GI microbiota has shown the ability to partially restore altered stress responses. Notably, when fecal microbiota from individuals with depression was transplanted into microbiota-deficient rats, it resulted in the transfer of a depressive behavioral phenotype. These findings suggest a connection between the GI microbiota and physiological stress mechanisms, with the potential to influence behavior in mice. Conversely, clinical studies have revealed that individuals with mood disorders exhibit altered gut microbiotas. In a similar vein, transferring microbiota-deficient rats with fecal microbiota transplantation led to the development of depressive behavioral phenotypes [21].

Nonetheless, the precise influence of GI microbiota on individuals' emotional well-being has yet to be fully elucidated. A consensus regarding the representation of altered microbial groups in individuals with depression has not been reached [22,23]. In addition, recent research on women without psychiatric illnesses did not establish statistically significant links between mood and GI microbiota [24]. These inconsistencies may be partially explained by variations in dietary intake patterns [2,22].

In light of the discussion above, conducting a comparative study examining the general psychopathological characteristics of patients with digestive (gastrointestinal) problems compared to a healthy control group holds significant importance. Such a

study would offer initial insights into the mental health profile of individuals facing digestive difficulties, as well as the correlations between psychological characteristics within this group. Therefore, the primary objective of this research was to explore how the mental health of patients with digestive issues differs from that of the healthy control group and, more specifically, to identify the psychopathological characteristics that distinguish between these two groups.

2. Methods

Considering the nature of the subject and the research problem, the present study adopts a comparative descriptive approach, retrospectively comparing two groups: gastrointestinal patients and healthy individuals. Convenience sampling was employed to select participants. After obtaining their consent, a total of 70 gastrointestinal patients and 70 healthy individuals with similar backgrounds in terms of age, gender, and level of education were recruited from gastroenterologists' clinics and internal medicine practices. The information for this research was collected through fieldwork, utilizing The Symptom Checklist-90-R (SCL-90-R) questionnaire.

The SCL-90-R questionnaire, consisting of 90 questions and nine scales, is a widely utilized tool for self-reporting psychological distress, various facets of psychopathological symptoms, and additional miscellaneous items. The scales encompassed within the SCL-90-R include a depression scale with 13 items, an aggression scale with six items, a physical activity scale with 12 items, a sensitivity scale in social relationships with nine things, a paranoid thoughts scale with six items, an obsession scale with ten items, an anxiety scale with ten items, a phobia scale with seven items, and a psychosis scale with ten things.

The participants' responses are assessed using a five-point Likert scale that includes the following response options: none, a little, to some extent, a lot, and incredibly. The corresponding scoring for these options is 0 to 4, respectively. In the SCL-90-R mental health questionnaire scoring system, the values are interpreted as follows: 0 represents none, indicating that the specific issue has never been a problem or bother for the participant; 1 corresponds to low, indicating that the problem or issue is minimal for the individual.

However, it exists and has caused me some discomfort (I have encountered it once or twice in the last two months); 2 corresponds to a certain extent: it indicates that this issue has arisen for me to a moderate degree, causing me distress. (For instance, I have experienced this problem three or four times in the past few weeks); 3 represents a lot: it signifies that this problem or issue has occurred frequently (for instance, once every two or three days) and with significant intensity, leading to considerable discomfort; 4 stands for extremely: this means that this issue or problem has arisen for me almost daily and with immense intensity, greatly upsetting me.

The reliability and validity of the SCL-90-R questionnaire in Iran have been reported to exceed 0.90. Marashi conducted a study where the reliability coefficient of this test was calculated using Cronbach's alpha method, resulting in values ranging from 0.80 to 0.93. Additionally, the reliability coefficient was reported to be between 0.68 and 0.81. The validity coefficient of the test, determined through the retest method, falls within the range of 0.38 to 0.66. In the present study, Cronbach's alpha was calculated for this test and yielded a reliability coefficient of 0.96, indicating a high level of reliability [25].

3. Results

The average age of the healthy individuals was 38.03 years, with a standard deviation of 9.02. However, on the opposite side, the average age of individuals with gastrointestinal problems was 39.23 years, with a standard deviation of 9.98. Both groups had participants ranging from undergraduate to doctoral education levels.

Variables	Group	Average	standard deviation	highest score	lowest score
SCL-90-R total score	patient	109.17	41.96	217	23
	healthy	83.91	53.91	193	0
Depression	patient	17.27	7.62	37	0
	healthy	12.95	9.97	33	0
Aggression	patient	8.64	4.15	23	0
	healthy	7.05	4.39	18	0
Somatization	patient	16.78	8.68	41	5
	healthy	13.13	9.86	38	0
Sensitivity in social relationships	patient	12.72	5.47	26	3
	healthy	10.63	6.46	28	0
Paranoid thoughts	patient	8.28	3.95	16	0
	healthy	6.8	4.94	18	0

Obsession	patient	14.07	5.02	26	6
	healthy	12.05	6.48	27	0
Anxiety	patient	12.19	6.03	32	0
	healthy	9.15	7.45	27	0
Phobia	patient	8.74	3.72	18	0
	healthy	5.41	5.12	19	0
Dissociation	patient	10.43	5.7	34	0
	healthy	6.7	6.23	27	0

Table 1: Mean and standard deviation of clinical features scores in patients with gastrointestinal problems and healthy people in the subscales of SCL-90-R

Table 1 displays the mean and standard deviation scores of psychopathological characteristics and their respective subscales in the two groups: patients with gastrointestinal problems and the healthy control group.

Before conducting the multivariate analysis of variance (MANOVA) to examine the difference of means, it is crucial to verify certain assumptions of the statistical analysis. These assumptions include the normal distribution of variables, homogeneity of variances, and a uniform variance-covariance matrix across all levels of the independent variable.

Based on the results of the investigation, it has been determined that the assumptions hold true, allowing for the appropriate inferential analysis to be carried out confidently

Test	value	F	df (Hypothesis)	df (Error)	p-values
Pillai effect	0.168	2.92	9	130	0.003
Wilks Lambda	0.832	2.92	9	130	0.003
hoteling's trace	0.202	2.92	9	130	0.003
Roy's Largest Root	0.202	2.92	9	130	0.003

Table 2: The results of multivariate analysis of variance tests of the dimensions of clinical characteristics in patients with gastrointestinal problems and healthy people

The results from Table 2 of the multivariate analysis of variance (MANOVA) indicate a significant difference between the two groups, individuals with gastrointestinal problems and healthy individuals, in at least one of the dependent variables. The statistical tests reveal a significant finding ($p < 0.01$) with an F-value of (130.9, 2/92).

Variable	source	sum of squares	mean square	F	p-values	size effect	df
depression	Group	655.92	655.92	8.329	0.005	0.057	1
	Error	10867.17	78.74				138
	Total	43509.23					140
aggression	Group	89.26	89.26	4.879	0.029	0.034	1
	Error	2524.65	18.29				138
	Total	11240.83					140
Somatization	Group	466.02	466.02	5.397	0.022	0.038	1
	Error	11915.88	86.54				138
	Total	43709.41					140
Sensitivity in social relationships	Group	153.73	153.73	4.283	0.040	0.030	1
	Error	4953.25	35.89				138
	Total	24202.50					140

Paranoid thoughts	Group	76.41	76.41	3.812	0.053	0.027	1
	Error	2766.14	20.04				138
	Total	10819.91					140
Obsession	Group	141.79	141.79	4.213	0.042	0.030	1
	Error	4644.74	33.65				138
	Total	28687.11					140
Anxiety	Group	324.01	324.01	7.035	0.009	0.049	1
	Error	6355.67	46.05				138
	Total	22637.02					140
Phobia	Group	388.38	388.38	19.336	0.001>	0.123	1
	Error	2771.91	20.08				138
	Total	68/10184					140
Dissociation	Group	486.80	486.80	13.636	0.001>	0.090	1
	Error	4926.76	35.7				138
	Total	15690.12					140

Based on the results presented in Table 3, there is a significant difference between individuals with gastrointestinal problems and the healthy group in various characteristics. Specifically, there is a significant difference in depression ($p < 0.01$, $F = 8.329$), aggression ($p < 0.01$, $F = 4.879$), somatization ($p < 0.01$, $F = 5.397$), sensitivity in social relations ($p < 0.01$, $F = 4.283$), obsession ($p < 0.05$, $F = 4.213$), anxiety ($p < 0.01$, $F = 7.035$), phobia ($p < 0.001$, $F = 19.336$), and psychosis ($p < 0.001$, $F = 13.636$).

By examining the average scores of these clinical characteristics in Table 1, it is evident that the group with gastrointestinal problems generally exhibits higher scores in these eight characteristics than the healthy group. However, based on the findings in Table 3, the two groups did not show a significant difference except for the characteristic of paranoid thoughts ($p < 0.053$, $F = 3.812$).

4. Discussion

In this study, researchers examined the psychological characteristics of individuals with digestive disorders compared to a healthy group. The findings revealed that individuals with digestive disorders scored higher on various psychological factors, including depression, aggressiveness, somatization, social sensitivities, preoccupations, anxiety, phobias, and psychosis, when compared to healthy participants. However, no statistically significant difference was observed in paranoid thoughts between the two groups.

Consistent with the findings of this study, previous research by Alander et al.26 has demonstrated that patients with digestive diseases tend to report higher levels of stress and psychological issues compared to healthy individuals. Health experts emphasize the strong connection between the brain and the stomach, acknowledging the direct influence of one on the other. Gastrointestinal disorders often manifest as chronic symptoms such as diarrhea, nausea, vomiting, irritable bowel, or stomach pain. Commonly, Individuals experiencing these persistent symptoms face psychological problems and stress. In support of this, Benner et al.27 also discovered that stress plays a significant role in predicting the severity of gastrointestinal disorders among patients.

Numerous studies have provided evidence of a comorbidity between psychopathological characteristics and digestive problems. Among these, depression and anxiety disorders stand out as the most prevalent psychiatric conditions in patients with functional gastrointestinal disorders [28]. The findings of this research indicate that functional gastrointestinal symptoms can independently predict depression in older individuals. Previous studies have also suggested that conditions like reflux syndrome, stomach discomfort, and indigestion may serve as predictors of depression in old age [29]. The association between certain stomach ailments, such as irritable bowel syndrome, and depression or anxiety has garnered significant attention. However, empirical investigations exploring this relationship remain scarce [30]. It has been observed that the severity of depressive symptoms and anxiety levels are correlated with the overall burden of gastrointestinal symptoms. The gut-brain axis refers to the bidirectional communication and interplay between the nervous, endocrine, and immune systems of the gastrointestinal and brain systems [31].

The present study reveals a higher prevalence of obsessive-compulsive symptoms and signs in patients with digestive problems than in their healthy counterparts. While anxiety is a prominent feature of this disorder, the relationship between obsessive-compulsive symptoms and digestive issues remains unclear. Interestingly, there is a notable research gap in the literature regarding the investigation of obsessive-compulsive disorder in gastrointestinal patients. However, studies have examined the presence of digestive problems in individuals with obsessive-compulsive disorder. For instance, patients with anorexia nervosa

often exhibit comorbid psychiatric conditions such as depression, obsessive-compulsive disorder, and personality disorders [32]. In another study by Turna et al., adult patients with obsessive-compulsive disorder were compared to matched control groups based on their gastrointestinal symptoms [33]. The researchers concluded that gastrointestinal symptoms should be considered in the clinical management of obsessive-compulsive patients due to their high prevalence and severity.

A recent study by Colligen sheds light on various clinical scenarios where gastrointestinal symptoms and psychosis often occur together, emphasizing the practical implications of this association [34]. The suspected link between the central nervous system and the gut has long been recognized, and there is a growing interest in investigating the gut microbiome in schizophrenia [35]. While gastrointestinal issues are commonly observed in individuals with schizophrenia, it is essential to note that gastrointestinal dysfunction and psychotic symptoms can also co-occur in the context of various medical and neurological conditions that have the potential to manifest both sets of symptoms. This co-occurrence extends across multiple diagnostic categories, including rare genetic disorders, autoimmune disorders, infectious diseases, endocrine disorders, neoplastic conditions, nutritional deficiencies, epilepsy, and different headache syndromes [36].

5. Conclusions

In conclusion, the findings of this study support the notion that patients with gastrointestinal diseases, particularly those affecting the intestines and stomach, have a higher prevalence of psychological and cognitive problems. These results align with the concept of altered brain-gut interactions and the communication within the brain-gut axis, providing empirical evidence for the impact of gastrointestinal disturbances on mental well-being.

The observed psychological and cognitive difficulties in these patients have significant implications for both psychiatric and digestive healthcare. The findings highlight the importance of recognizing the shared etiology between psychiatric disorders and gastrointestinal conditions. By understanding the complex interplay between the brain and the gut, healthcare professionals can gain insights into the underlying mechanisms that contribute to the co-occurrence of these issues. This knowledge can inform the development of more comprehensive treatment approaches that address both the psychiatric and digestive aspects of patients' health.

Moreover, these findings have important therapeutic implications. Taking an integrated approach to care, which acknowledges the bidirectional relationship between mental health and gastrointestinal health, can lead to better outcomes for patients. Interventions targeting the gut microbiota, such as the use of probiotics or dietary modifications, have the potential to not only alleviate gastrointestinal symptoms but also positively impact psychiatric symptoms. Similarly, addressing psychological factors such as stress management and psychotherapy can benefit mental health and gastrointestinal functioning.

By recognizing the interconnected nature of psychiatric and digestive problems and incorporating this understanding into clinical practice, healthcare providers can offer more comprehensive and tailored care to patients. This integrated approach has the potential to enhance the overall well-being of individuals with gastrointestinal diseases and contribute to advancements in the treatment of both psychiatric and digestive disorders.

References

1. Cussotto, S., Sandhu, K. V., Dinan, T. G., & Cryan, J. F. (2018). The neuroendocrinology of the microbiota-gut-brain axis: a behavioural perspective. Frontiers in neuroendocrinology, 51, 80-101.
2. Evans, J. M., Morris, L. S., & Marchesi, J. R. (2013). The gut microbiome: the role of a virtual organ in the endocrinology of the host. J Endocrinol, 218(3), R37-47.
3. Frank, D. N., & Pace, N. R. (2008). Gastrointestinal microbiology enters the metagenomics era. Current opinion in gastroenterology, 24(1), 4-10.
4. Sarkar, A., Lehto, S. M., Harty, S., Dinan, T. G., Cryan, J. F., & Burnet, P. W. (2016). Psychobiotics and the manipulation of bacteria–gut–brain signals. Trends in neurosciences, 39(11), 763-781.
5. Luczynski, P., McVey Neufeld, K. A., Oriach, C. S., Clarke, G., Dinan, T. G., & Cryan, J. F. (2016). Growing up in a bubble: using germ-free animals to assess the influence of the gut microbiota on brain and behavior. International Journal of Neuropsychopharmacology, 19(8), pyw020.
6. Capuco, A., Urits, I., Hasoon, J., Chun, R., Gerald, B., Wang, J. K., ... & Viswanath, O. (2020). Current perspectives on gut microbiome dysbiosis and depression. Advances in therapy, 37, 1328-1346.
7. Matsumoto, M., Kibe, R., Ooga, T., Aiba, Y., Sawaki, E., Koga, Y., & Benno, Y. (2013). Cerebral low-molecular metabolites influenced by intestinal microbiota: a pilot study. Frontiers in systems neuroscience, 7, 9.
8. Lyte, M. (2013). Microbial endocrinology in the microbiome-gut-brain axis: how bacterial production and utilization of neurochemicals influence behavior. PLoS pathogens, 9(11), e1003726.
9. Wang, B., Mao, Y. K., Diorio, C., Pasyk, M., Wu, R. Y., Bienenstock, J., & Kunze, W. A. (2010). Luminal administration ex vivo of a live Lactobacillus species moderates mouse jejunal motility within minutes. The FASEB Journal, 24(10), 4078-4088.
10. Cryan, J. F., O'Riordan, K. J., Cowan, C. S., Sandhu, K. V., Bastiaanssen, T. F., Boehme, M., ... & Dinan, T. G. (2019). The microbiota-gut-brain axis. Physiological reviews.
11. Horn, J., Mayer, D. E., Chen, S., & Mayer, E. A. (2022). Role of diet and its effects on the gut microbiome in the pathophysiology of mental disorders. Translational psychiatry,

12(1), 164.
12. Sichetti, M., De Marco, S., Pagiotti, R., Traina, G., & Pietrella, D. (2018). Anti-inflammatory effect of multistrain probiotic formulation (L. rhamnosus, B. lactis, and B. longum). Nutrition, 53, 95-102.
13. Petersen, C., & Round, J. L. (2014). Defining dysbiosis and its influence on host immunity and disease. Cellular microbiology, 16(7), 1024-1033.
14. Shahbazi, R., Yasavoli-Sharahi, H., Alsadi, N., Ismail, N., & Matar, C. (2020). Probiotics in treatment of viral respiratory infections and neuroinflammatory disorders. Molecules, 25(21), 4891.
15. Rinninella, E., Raoul, P., Cintoni, M., Franceschi, F., Miggiano, G. A. D., Gasbarrini, A., & Mele, M. C. (2019). What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms, 7(1), 14.
16. Villanueva-Millán, M. J., Pérez-Matute, P., & Oteo, J. A. (2015). Gut microbiota: a key player in health and disease. A review focused on obesity. Journal of physiology and biochemistry, 71, 509-525.
17. Carding, S., Verbeke, K., Vipond, D. T., Corfe, B. M., & Owen, L. J. (2015). Dysbiosis of the gut microbiota in disease. Microbial ecology in health and disease, 26(1), 26191.
18. Gao, J., Xu, K., Liu, H., Liu, G., Bai, M., Peng, C., ... & Yin, Y. (2018). Impact of the gut microbiota on intestinal immunity mediated by tryptophan metabolism. Frontiers in cellular and infection microbiology, 8, 13.
19. McGuinness, A. J., Davis, J. A., Dawson, S. L., Loughman, A., Collier, F., O'hely, M., ... & Jacka, F. N. (2022). A systematic review of gut microbiota composition in observational studies of major depressive disorder, bipolar disorder and schizophrenia. Molecular psychiatry, 27(4), 1920-1935.
20. Taylor, A. M., Thompson, S. V., Edwards, C. G., Musaad, S. M., Khan, N. A., & Holscher, H. D. (2020). Associations among diet, the gastrointestinal microbiota, and negative emotional states in adults. Nutritional neuroscience, 23(12), 983-992.
21. Jiang, H., Ling, Z., Zhang, Y., Mao, H., Ma, Z., Yin, Y., ... & Ruan, B. (2015). Altered fecal microbiota composition in patients with major depressive disorder. Brain, behavior, and immunity, 48, 186-194.
22. Zheng, P., Zeng, B., Zhou, C., Liu, M., Fang, Z., Xu, X., ... & Xie, P. (2016). Gut microbiome remodeling induces depressive-like behaviors through a pathway mediated by the host's metabolism. Molecular psychiatry, 21(6), 786-796.
23. Kleiman, S. C., Bulik-Sullivan, E. C., Glenny, E. M., Zerwas, S. C., Huh, E. Y., Tsilimigras, M. C., ... & Carroll, I. M. (2017). The gut-brain axis in healthy females: lack of significant association between microbial composition and diversity with psychiatric measures. PloS one, 12(1), e0170208.
24. Obeiri, A., Fatemeh., Mohammadreza, S. (2019). Validation and validation of the Symptom List (SCL-90-R) and Short Symptom Questionnaire (BSI-53). Clinical Psychology and Personality, 17(2), 169-195.
25. Ålander, T., Svärdsudd, K., Johansson, S. E., & Agréus, L. (2005). Psychological illness is commonly associated with functional gastrointestinal disorders and is important to consider during patient consultation: a population-based study. BMC medicine, 3(1), 1-12.
26. Bener, A., OAA Al-Hamaq, A., & E Dafeeah, E. (2011). High prevalence of depression, anxiety and stress symptoms among diabetes mellitus patients. The Open Psychiatry Journal, 5(1).
27. Van Oudenhove, L., Levy, R. L., Crowell, M. D., Drossman, D. A., Halpert, A. D., Keefer, L., ... & Naliboff, B. D. (2016). Biopsychosocial aspects of functional gastrointestinal disorders: how central and environmental processes contribute to the development and expression of functional gastrointestinal disorders. Gastroenterology, 150(6), 1355-1367.
28. Pilichiewicz, A. N., Horowitz, M., Holtmann, G. J., Talley, N. J., & Feinle–Bisset, C. (2009). Relationship between symptoms and dietary patterns in patients with functional dyspepsia. Clinical Gastroenterology and Hepatology, 7(3), 317-322.
29. Cantarero-Prieto, D., & Moreno-Mencia, P. (2022). The effects of gastrointestinal disturbances on the onset of depression and anxiety. PloS one, 17(1), e0262712.
30. Rea, K., Dinan, T. G., & Cryan, J. F. (2020). Gut microbiota: a perspective for psychiatrists. Neuropsychobiology, 79(1), 50-62.
31. O'Brien, K. M., & Vincent, N. K. (2003). Psychiatric comorbidity in anorexia and bulimia nervosa: nature, prevalence, and causal relationships. Clinical psychology review, 23(1), 57-74.
32. Turna, J., Kaplan, K. G., Patterson, B., Bercik, P., Anglin, R., Soreni, N., & Van Ameringen, M. (2019). Higher prevalence of irritable bowel syndrome and greater gastrointestinal symptoms in obsessive-compulsive disorder. Journal of psychiatric research, 118, 1-6.
33. Colijn, M. A. (2022). The co-occurrence of gastrointestinal symptoms and psychosis: diagnostic considerations. The Primary Care Companion for CNS Disorders, 24(3), 41541.
34. Liu, J. C., Gorbovskaya, I., Hahn, M. K., & Müller, D. J. (2021). The gut microbiome in schizophrenia and the potential benefits of prebiotic and probiotic treatment. Nutrients, 13(4), 1152.
35. Söderquist, F., Syk, M., Just, D., Kurbalija Novicic, Z., Rasmusson, A. J., Hellström, P. M., ... & Cunningham, J. L. (2020). A cross-sectional study of gastrointestinal symptoms, depressive symptoms and trait anxiety in young adults. BMC psychiatry, 20, 1-10.