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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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THE GUT-BRAIN AXIS: IMPLICATIONS FOR NEUROLOGICAL DISORDERS, MENTAL HEALTH, AND IMMUNE FUNCTION

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Abstract.

A gut-brain axis (GBA) has a long history of conceptual development. Intestinal dysbiosis has now been recognized as a key player in the development of adult neurodevelopmental disorders, obesity, and inflammatory bowel disease. Recent developments in metagenomics suggest those nutrition and gut microbiotas (GM) are important regulators of the gut-brain communication pathways that cause neurodevelopmental and psychiatric problems in adulthood. Intestinal dysbiosis and neurodevelopmental disease outcomes in preterm newborns are being linked by recent research. Recent clinical investigations demonstrate that in critical care units, intestinal dysbiosis occurs before late-onset newborn sepsis and necrotizing enterocolitis. Strong epidemiologic data also shows a connection between necrotizing enterocolitis and extremely low birth weight babies' long-term psychomotor impairments and late-onset neonatal sepsis. The GBA theory suggests that intestinal bacteria may indirectly affect preterm newborns' developing brains. In this review, we emphasize the structure and function of the GBA and discuss how immune-microbial dysfunction in the gut affects the transmission of stress signals to the brain. Preterm babies who are exposed to these signals develop neurologic disorders. Understanding neuronal and humoral communication through the GBA may provide insight into therapeutic and nutritional strategies that may enhance the results of very low-birth-weight babies.

Key words. Neurological Disorders (ND), Immune Function (IF), Gut Microbiotas (GM), Gut-Brain Axis (GBA), Mental Health.

Introduction.

GBA refers to the two-way communication system between the gastrointestinal (GI) tract, and central nervous system (NS), involving neural, immunological pathways, and hormonal. This communication plays a crucial role in various aspects of human health, including neurological disorders (ND), mental health, and immune function (IF) [1]. In ND, Emerging research suggests that disruptions in the GBA may give to the enlargement and progression of ND. For example, studies have found associations between gut dysbiosis (imbalances in the gut microbial community) and multiple sclerosis [2]. The GM can produce and regulate various neurotransmitters, including dopamine, serotonin, and gamma-aminobutyric acid (GABA), which are involved in ND functioning [3]. In Mental Health, The GBA has profound implications for mental health conditions such as depression, anxiety, and stress-related disorders [4]. The GM influences the production of neurotransmitters and neuroactive compounds that impact mood and behavior [5]. In IF, The IF growth and operation are significantly influenced by the GM. A significant fraction of IF is nearby in the gut-associated lymphoid tissue (GALT), which is continually exposed to antigens produced from the GM. Interactions between the GM and the IF help establish IF tolerance and prevent the development of autoimmune diseases. Disruptions in the GM composition, such as dysbiosis or increased intestinal permeability (leaky gut), can lead to IF dysregulation and inflammation, which have been implicated in various diseases, including autoimmune disorders and allergic conditions [6-8]. The GBA refers to the two-way statement system connecting the gastrointestinal tract (the gut) and intelligence. This axis involves a complex network of connections between the gut, the autonomic NS, the enteric NS, and the central NS [9]. The gut and the brain are constantly exchanging signals and information through various pathways, including neural, hormonal, and IF pathways. This communication stage is essential to position in maintaining the overall physical condition and has implications for ND, mental health, and IF [10]. The GM communicates through the mind in the course of the vagus nerve, a major pathway for bidirectional signaling. This connection enables the GM to influence brain function and emotional states. Studies have shown that manipulating GM through interventions like probiotics and fecal microbiota transplantation can have beneficial effects on mental health symptoms [11]. Moreover, GM can modulate the resistant reaction by influencing the production and function of resistant cells and resistant molecules. This IF modulation can have far-reaching effects on overall health and may influence the expansion and sequence of immune-related disorders [12]. The GBA is a complex and dynamic system that plays a crucial role in ND, mental health conditions, and IF [13]. Accepting the connections between the gut & the brain can provide insights into the underlying mechanisms of these conditions and potentially lead to novel therapeutic approaches targeting the GM and the GBA [14]. In the study [15], the complicated interactions of the microbiota GBS are examined to better understand the pathogenesis caused by the microbiota, the potential for noninvasive prognosis, and treatment options that take advantage of modulations of the microbiota GBA. Furthermore, they analyze the shortcomings of present strategies and give insights into the continuing shift from the bench to the bedside. Higher fiber diets have been shown to increase the variety and abundance of beneficial taxa in GM as well as butyrate synthesis, which has been shown to

have neuroprotective effects and improve the plasticity of neurons. The article [16] provided insight into how gender variations in the GBA may be responsible for the disparities involving male and female prevalence of psychiatric, neurodevelopmental, and neurodegenerative illnesses. They concentrate on conditions including anxiety disorders, autism spectrum disorder, psychotic disorders, stress, and Parkinson's disease. Study [17] examined the GBA through the lens of stress and how stress may affect a person's physiology from the time of conception until maturity. There are several mechanisms through which microbiome changes generate shifts in behavior. Inflammation in the stomach has effects on the brain as well, and a comparable systemic reaction is seen. Study [18] described the pathophysiological processes resulting from disturbance of the MGB axis and potential treatment strategies, with a particular emphasis on the complex network's GM. The development of novel medicines for enhancing the therapeutic care of these patients may be aided by an understanding of the processes governing the GM and its mutual connections by the resistant and other systems. Additionally, the blow of psychiatric medications on top of the GM presently being utilized in patients as well as potential therapeutical techniques focusing on this environment will be taken into consideration. Natural polysaccharides are critical for preserving the regular state of gut flora, according to the research that has been conducted so far. The study's findings, which include the modulatory role of plant polysaccharides on gut flora and the two-way communication between the GM and the brain, provide fresh insights into how to prevent and cure neurodegenerative illnesses [19]. Article [20] discussed the changes in GM that take place during depressive states, the relationship between these changes and depressive-like behavior, the possible apparatus connecting disruption in GM to depression, and the earliest attempts to use GM intervention for the treatment of depression. Study [21] provided a general overview of GM, paying close attention to mast cells and ND. Mast cells serve as sensors and effectors of cytokines and neurotransmitters, which have important roles in neuroimmune communication. Probiotic use in this situation may be a good therapeutic strategy to use in conjunction with conventional treatments. To determine if the gut bacteria cause ND or whether such conditions affect the bacterial composition, further research must be done. In Study [22], they summarise the most recent evidence that the protected organization and GM take part in important roles in the conservation of brain performance and the emergence of ND. Additionally, they present the latest developments in the GBA idea for treating ND using probiotics and faucal microbiota transplants. In a study [23], they evaluated molecular networks through which the microbiota, gut, and GBA control brain growth and purpose, and the potential roles for these networks in ND associated with immunological dysfunction. Although several studies have looked into the microbiota-GBA, there are still difficulties in applying the results of these studies to people because of the intricate interactions between the GM and the brain. Study [24] focused on the two-way announcement among the stomach and brain, its effects & functions in the regulation of different ND, such as anxiety, depression, and schizophrenia, and makes an effort to investigate the fundamental apparatus on behalf of the equal. Animal models for studying the masterpiece of the intestinal microbiota, research on the impact of bacteria spreading from faces, and germ-free mice Study [25] evaluated the search of computational analysis approaches that can help to comprehend the relationship between the microbiome, the gut, and the brain, as well as the causes and development of neurological disorders, using a systems ecology perspective. A shotgun approach and high-throughput sequencing of healthy and neurological condition specimens recorded in biological databases generated large amounts of microbiological 16S ribosomal RNA sequence data that provided here together with the bioinformatics instruments employed to determine such relationships. The study [26] provided the disciplines of gastroenterology and neuroscience with the purpose of demonstrating that the gut-brain relation can lead to the establishment of a number of neurological diseases. They discussed the most recent information on how microbial imbalance contributes to neurodegeneration and neuroinflammatory disorders like Alzheimer's, Parkinson's, and multiple sclerosis.

The gut-brain axis.

The GBA is defined as the communication pathway between the motor and sensory components of the gastrointestinal tract and the central NS. Figure 1 demonstrates the intricacy, moderators, and multiorgan linkages of GBA-related signaling pathways that affect the balance between health and sickness in a preterm baby.

The brain, which connects the hypothalamic-pituitary-adrenal axis, limbic system, brain stem, and cerebral cortex, is the main part of the GBA. The limbic cortex controls smell and unifies sensory and motor processes. Other parts of the brain that control a variety of actions provide information to the limbic system. Studies on the effects of pain and maternal deprivation on newborn mice have shown that the limbic system is crucial to the hippocampus' development. Damage to the hippocampus in premature babies without cerebral hemorrhage is presumably the source of neurobehavioral problems documented in these children throughout childhood. When studying limbic system impairments in human preterm babies, researchers must account for gender differences in the impact of stress. Through the sympathetic, autonomic, and enteric nervous systems (ENS), the peripheral parts of the GBA connect with the brain. The ENS, via which gut bacteria may influence brain growth and function, has been shown to impact neuronal signals. The ENS is an intricate network of nerves and cells that lines the interior of the gut wall. Diseases of the newborn that affect the ENS are discussed in the context of GBA. The GBA includes peripheral components for the autonomic NS, the sympathetic NS, and the hypothalamic-pituitary axis. A significant retrograde communication pathway from the stomach to the brain is the afferent vagus nerve. The intestinal epithelial barrier function may be lost as a consequence of this inflammation, allowing for bacterial invasion. Increased intestinal permeability leads to gastric inflammation by simultaneously activating the immune. Changes in brain function and illness are brought on by signals that the GBA transmits to the intestinal and systemic IF. The ENS, the autonomic NS, and the hypothalamic-pituitary

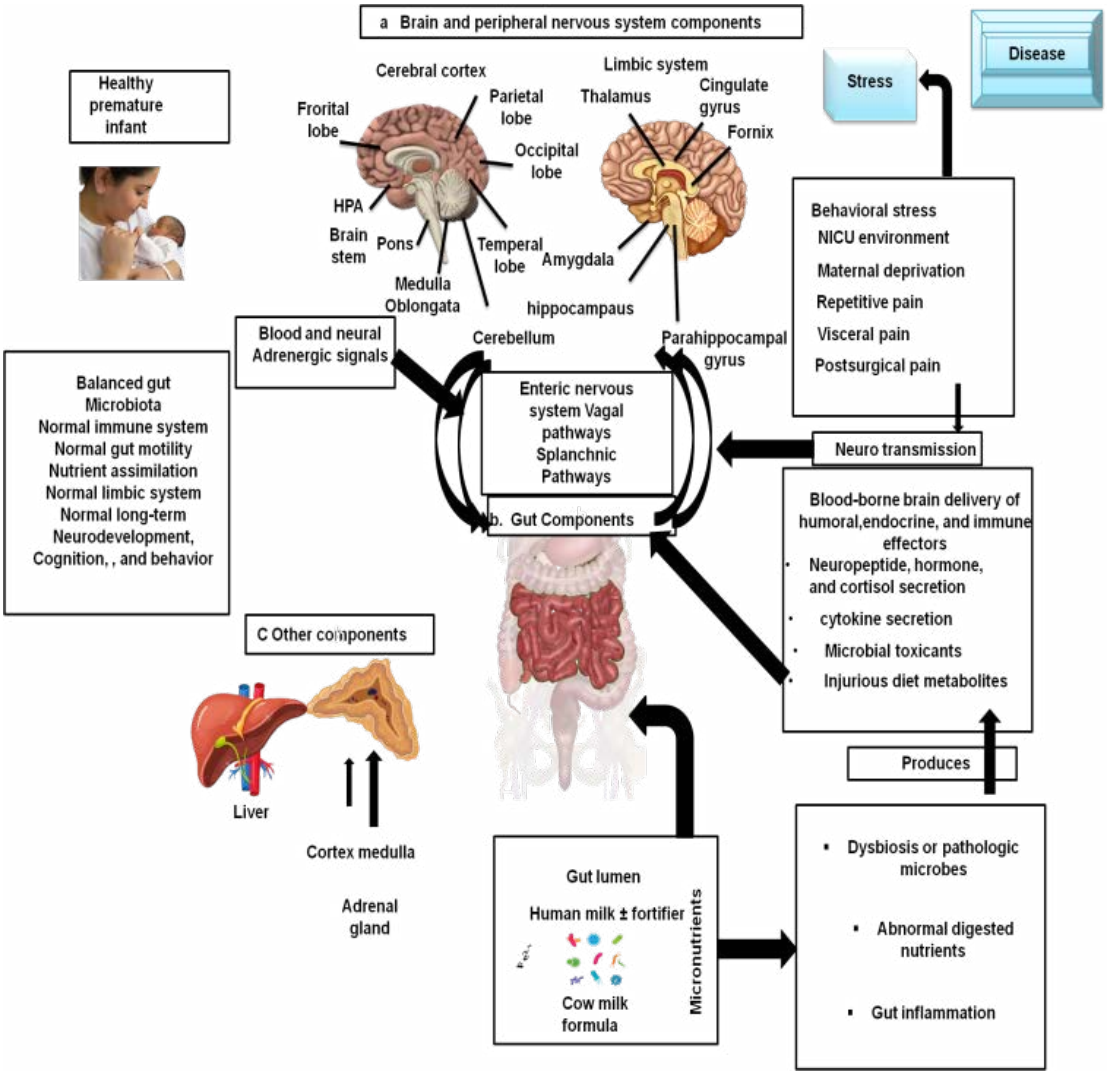

Figure 1. *The GBA's brain, peripheral nerve networks, and gut parts are depicted in the figure's center.*

axis all provide messages to the limbic system and the brain about nutrition and microorganisms in the intestine. The brain stems and higher cortical areas like the limbic system, which is involved in rewards, are connected reciprocally through the hypothalamus. Hormone and neuropeptide production in the stomach during a stressful situation eventually triggers the gland through signals sent to the brain. Apparatus of the GBA linked include peptide YY, pancreatic polypeptide, glucagon-like peptide-1, and oxyntomodulin, whereas fasting increases ghrelin production. With the help of neuropeptide signals, the GBA also affects intestinal IF. Dendritic cells' and T cells' respective roles in the brain, in secondary lymphoid organs like Peyer's patch, and the intestinal wall are all influenced by neuropeptides like vasoactive intestinal peptide and norepinephrine. Depending on the ratio of "neuropeptides and other immunomodulatory" substances, immune cells may either induce an inflammatory response to microbial and nutritional, hence guiding the formation of distinct effectors lymphocyte populations. NS has been linked to changes in the composition of the gut microbial community, which in turn has been linked to an impairment of barricade purpose and an increase in intestinal permeability.

Diseases associated with GBA disorders in the embryo and newborn.

Coordination of neuronal, intestinal motor and absorptive, and immunologic systems throughout pre- and postnatal life ensures a strong newborn baby and fosters continuing growth and development throughout immaturity and babyhood. Multiple interaction cells and organs contribute to a normal vs. dysfunctional GBA, which results in either health or illness (Figure 1). Pediatricians are aware of morphologic ENS deficiencies. Hirschsprung's disease, which increases the risk of enterocolitis, is brought on by ENS congenital abnormalities. Megalocystis, megacolon, and malrotation are all symptoms of the extremely deadly developmental disorder of the ENS known as intestinal neuronal dysplasia. "Myelomeningocele and acquired adult disorders" like acute spinal cord injury are linked to gut motor dysfunction. A nonanatomic, neurogenic intestinal obstruction condition is brought on by congenital or acquired disorders of the spinal cord that change ENS function. There are other things than congenital abnormalities that may happen to a fetus that influence how the ENS develops. When used during human pregnancy, selective serotonin reuptake

inhibitors (SSRIs) have sparked worries about the ENS developing abnormally. Investigations of infants who were exposed to SSRIs while they were still in the womb have shown eating problems, impaired motor function, and behavioral abnormalities; these results seem connected to anomalies in the autonomic NS. The signs of the baby being exposed to selective serotonin reuptake inhibitors during pregnancy include.

(i) Delayed infantile speech developmental milestones

(ii) Behavior issues that began after childhood.

We must find out more about the "defects" that pregnancy-related medications like valproic acid and SSRIs may introduce into the human fetal ENS. The pathophysiology of autism spectrum disorders (ASD) may be influenced by selective serotonin reuptake inhibitors used during pregnancy, albeit the mechanisms by which selective serotonin reuptake inhibitors alter NS development are currently poorly understood. Olanzapine, an antipsychotic medicine that balances the brain, was administered to rats. These outcomes included changed fecal microbiota composition, recruitment of macrophages into adipose tissue, and higher plasma stage of proinflammatory cytokines. This study discusses the link between prenatal selective serotonin re-uptake inhibitors exposure and autism spectrum disorders.

Interactions of GBA with gut microbioma, epidermis, and immune cells.

The physiological role of the GBA is examined concerning interactions between intestinal epithelia, GM, and the IF. Given their closeness, GM can activate and control intestinal IF and gut epithelia, and the ENS. Although there is a lack of primary research on this issue, a review explains the crucial involvement of intestinal microbiota in the postnatal increase of gastrointestinal processes in premature newborns. Recent research indicates an association between postnatal events, such as the use of antibiotics, and childhood obesity in infants and children. Obesity and GM are related because the latter tends to accumulate more energy. Research on identical twins has shown phylum-level differences in the GM between lean and obese individuals. These differences include lower bacterial diversity, altered gene representation in the microbiome, and abnormal metabolic pathways. Diet-related microbial indicators in the feces of obese people are associated with altered microbiota and poor metabolic health. Microbes in the gut might set the stage for efficient dietary energy salvage. One such bacterium is Faecalibacterium prausnitzii, which is often found in the intestines of overweight children in southern India and is known to enhance epithelial health. Beyond affecting obesity's pathophysiology, gut microorganisms also have an impact on the prevalence of diseases including type 2 diabetes, demyelinating disorders, mental illness, behavioral abnormalities, and irritable bowel syndrome. How dendritic cells, intestinal epithelia, and other underlying IF recognize commensal and pathogenic bacteria and how these cells communicate with one another. Dendritic cells process and display antigens as M cells cover Peyer's patches during the development of tolerance. Secretory IgA prevents intestinal epithelial invasion by binding to invading microorganisms in intestinal fluid and the mucin layer. In addition, the mucin layer contains antimicrobial peptides generated by enterocytes that prevent microbial penetration of the intestinal barrier. Intestinal lip polysaccharide binds Toll-like receptor-4 on enterocytes, which is produced by the cell walls of Enterobacteriaceae. Intestinal IF cells are activated to create cytokines in response to pathogen-associated molecular pattern recognition, which in turn triggers ND transmissions through the vagus nerve. Toxoplasma gondii infection causes ileitis in mice via activating Toll-like receptor-9 in the intestinal cells. The animals lacked cerebral, resulting in increased amounts of proinflammatory cytokines in their brain tissue. The findings of this research provide compelling evidence that pathogen-specific infection and inflammation in the gastrointestinal tract might trigger immune-mediated inflammation in the central NS. According to recent research, the inflammasome helps the gut's innate IF cells identify signals connected to bacteria and other types of harm. By acting on the hypothalamic-pituitary axis, the GBA may control the activation of gut innate IF cells through the inflammasome, therefore reducing inflammation. In numerous animal species, it has been shown that GM may transmit inflammation to the gut-brain axis. While interactions between Escherichia coli and the gut-brain axis convey an inflammatory reaction, F. prausnitzii, generates an anti-inflammatory reaction. Mucin synthesis by intestinal epithelia, a crucial human defense against microbial invasion, may be boosted by commensal flora to induce protective responses. In addition, B. thetaiotaomicron up-regulates the production of angiogenin4 in crypt Paneth cells, which serves as both an “antimicrobial peptide and an angiogenic” factor to promote the development and condition of the intestinal villi. Consequently, beneficial bacterium maintain health and balance in the growing digestive tract. Intestinal dysbiosis and intestinal inflammation define necrotizing enterocolitis (NEC), a disease that mostly affects premature infants. There is an increased risk for significant long-term neurodevelopmental problems when NEC worsens the hospital stay. Negative effects on brain function are mediated through the GBA due to the stress caused by NEC. Long-term psychomotor and intestinal impairments are associated with infections and intestinal damage lead to the release of microbial toxins and pro-inflammatory cytokines into following NEC. In NEC, oxidant stress and other mediators of brain damage are proportional to the severity of the intestinal injury. More study in newborns is needed to determine the involvement of the gut-brain axis in the etiology of cerebral palsy and autism spectrum disorders. However, intestinal inflammation during pregnancy may be triggered by both viral and noninfectious disorders. Infection and inflammation of the fetal intestines presuppose that germs are ingested by the baby before birth. Swallowing does not begin until about 29–31 weeks of pregnancy. Since premature labor is linked to the presence of the bacteria Ureaplasma parvum and Ureaplasma urealyticum, the general premise is accurate. Ureaplasma colonization of the respiratory tract in extremely premature newborns increases the risk of necrotizing enterocolitis. Changes in the intestinal microbiota and the resulting "dysbiosis" likely play a central role in the pathogenesis of NEC, although they occur after birth. Between 7 days and 72hr before the commencement of NEC cases, a

bloom or significant rise in the phylum Proteobacteria has been found in fecal samples. However, the research did not find a correlation between any specific genus or species and NEC in newborns. In extremely premature neonates, intestinal dysbiosis is a risk factor for the development of late-onset neonatal sepsis. Metagenomics has revealed these previously unknown aspects of the GM and the etiology of late-onset neonatal sepsis or NEC in extremely preterm newborns. The field of metagenomics examines the genes and metabolites produced by bacteria in a specific setting, such as the digestive tract. To determine the molecular fingerprints of bacteria in a given environment, analytical tools are used in metagenomic approaches. Software programs are used to analyze these signals, and their results define the microbial ecology of the samples' environments. Neonatal intensive care unit nurses and doctors may not be acquainted with the analytical tools, molecular procedures, bioinformatics, and data formats related to metagenomic research. Microbes in human newborn organs may be identified using culture-independent approaches, as described in a recent review of metagenomics. Interstitial cells of Cajal operate as the intestinal pacemaker, stimulating the muscularis mucosae at regular intervals. Pathogenic bacteria in the intestinal lumen may be eliminated with the aid of gut motility and feces. When a very premature newborn develops ileus, doctors should be on the lookout for signs that toxins in the gut are blocking the action of the interstitial cells of Cajal. The accompanying justification outlines the physiology, however, most neonatologists already know that an ileus is a warning sign of NEC. For proper formation and operation of both the gastrointestinal and systemic IF systems, GM is crucial. Pregnancy continuation and healthy development of the fetus are linked to a Th2:Th1 lymphocyte bias. The Th2 bias seen in newborns is likely a carryover from immunosuppression found in pregnant women. Researchers have shown that newborn mice are more vulnerable to infection because of the immunologic environment. Intestinal microbial colonization after birth is linked to a reduction in the risk of infection and an end to the neonatal Th2:Th1 imbalance. In light of the GBA theory, this work reviews a variety of neurologic repercussions of common intestinal illnesses; therefore, the list of stressors is by no means complete. We chose prenatal and postnatal stress conditions in the gut based on their relevance to GBA pathogenesis.

The study of the laws that govern psychological events and human behavior is the field of psychology. To make matters worse, it seems that the more we learn about human psychology, the more we discover how little we understand. Until very recently, there was not a single mental disease for which a reliable physiological, biochemical, or genetic biomarker had been developed. There is a noticeable gap in the field of psychology's practical application, and mental diseases continue to constitute significant medical obstacles. Table 1, 2, 3 and 4 depicts the dramatic rise in the healthcare burden caused by the rising prevalence of individuals with mental and neurological problems over the last several decades. Mental problems account for about 20% of all medical costs, while treatment and recovery rates are far lower than for other diseases. All of these results point to the idea that humans are super organisms,

Table 1. *Neurological and mental disorders increased medical expenses (DALYs and Collaborators).*

Disorder	Start date	End date	Participants
Neurological disorder	Jan 12, 2017	Mar 13,2018	60000
	Apr 10, 2018	June 21,2019	70000
	July 14, 2019	Aug 13, 2020	80000
	Sep 25, 2020	Apr 18, 2021	81000
	June 20, 2021	Mar 19, 2022	90000
Mental and Substance use disorders	Jan 16, 2017	Apr 14,2018	90000
	Apr 20, 2018	July 25,2019	300000
	July 28, 2019	Aug 10, 2020	500000
	Sep 18, 2020	Apr 3, 2021	140000
	June 15, 2021	Mar 22, 2022	140000

Table 2. *Disability-adjusted life years (DALYs) brought on, respectively, by mental and neurological disorders.*

	Mental and substance use disorders	Neurological disorders
2018	4.8	3.2
2019	5.5	3.5
2020	5.3	3.3
2021	5.4	3.6
2022	5.6	3.8

Table 3. *The number of DALYs in 2018, 2020, and 2022 brought on by different diseases.*

ADHD	1000
Motor neuron disease	2000
Multiple sclerosis	2000
Eating disorders	3000
Parkinson's disease	4000
Conduct disorder	6000
Tension-type headache	8000
Bipolar disorder	9000
Autistic spectrum disorders	10000

Table 4. *The DALYs brought on by different diseases in 2018, 2020, and 2022.*

Schizophrenia	10000
Alcohol use disorders	12000
Drug use disorders	20000
Alzheimer's and other dementias	30000
Anxiety disorders	28000
Depressive disorders	41000
Migraine	42000

which has been overlooked by previous studies. Neurological and mental disorders increased medical expenses (DALYs and Collaborators). Figure 2 displays the disability-adjusted life years (DALYs) brought on, respectively, by mental and neurological disorders. The DALYs caused by various illnesses in 2018, 2020, and 2022 are shown in Figure 3.

Newborn nutrition and GBA function changes.

Though beneficial for the IF system, microbial colonization of the gut also works in tandem with food to promote healthy brain development. Many beneficial bio elements for health

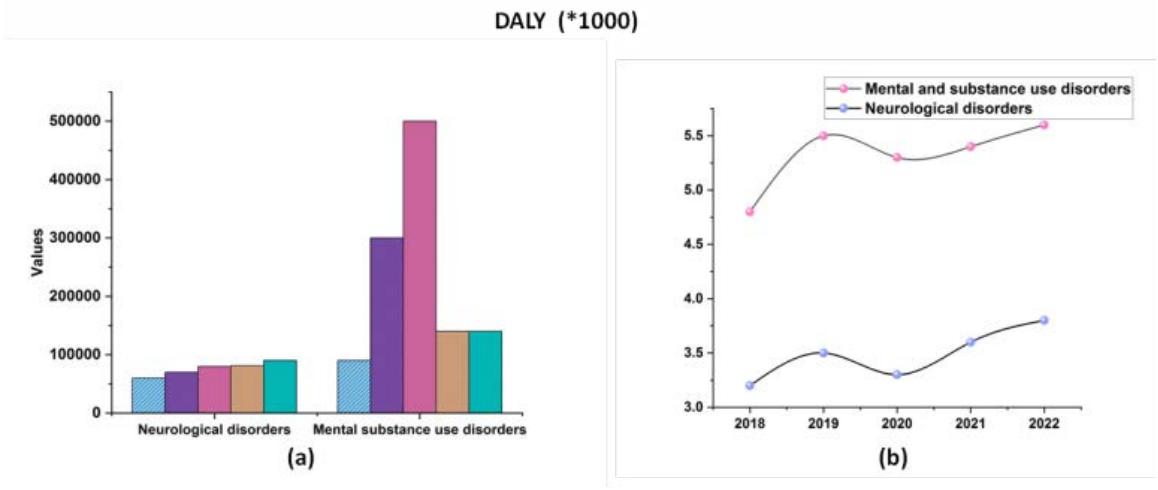

Figure 2. *Neurological and mental disorders increased medical expenses (DALYs and Collaborators).*

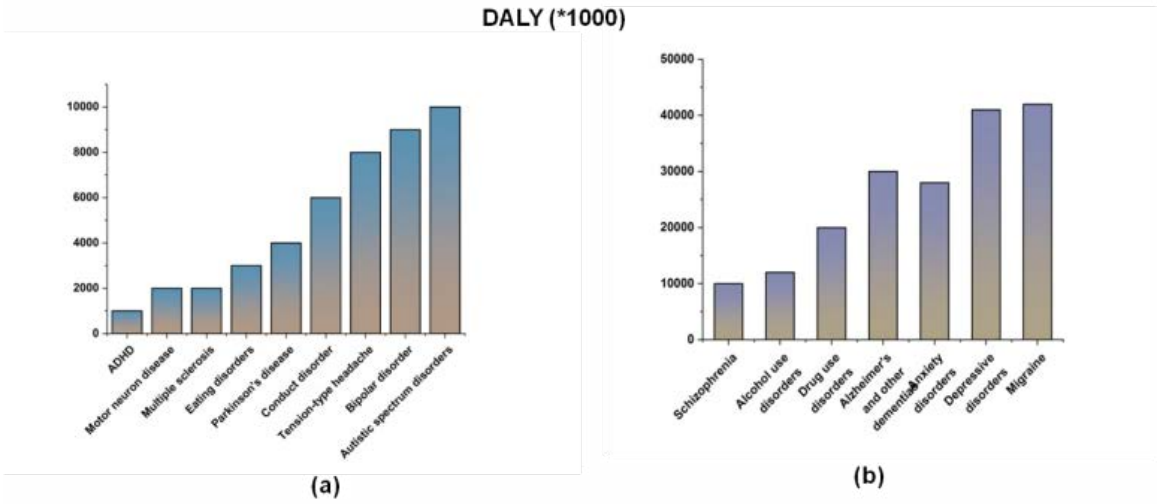

Figure 3. *The DALYs caused by various illnesses in 2018, 2020, and 2022.*

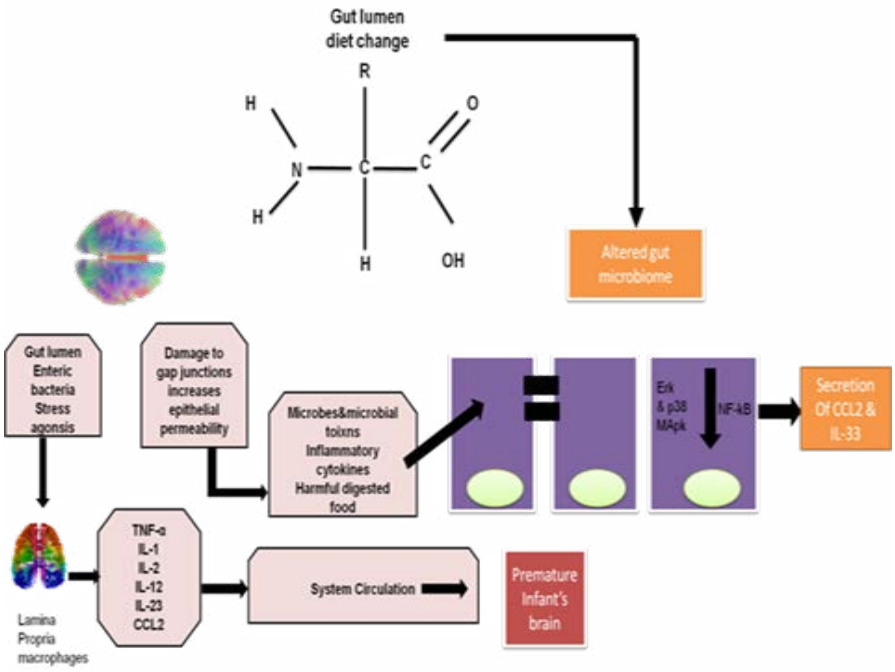

Figure 4. *Increased permeability and loss of the protective intestinal barrier.*

and brain development are found in human milk. Human milk's immunological qualities are preserved better by freezing than during pasteurization. NEC may be avoided because of the presence of lactoferrin, lysozyme, and other antimicrobial proteins and immunomodulatory substances in fresh colostrums and milk. NEC may be avoided in a rat newborn model by administering disialyllacto-Ntetraose, an oligosaccharide found in human milk. Human milk oligosaccharides help the developing digestive tract of premature newborns via many methods. Premature newborns that suffer from NEC, an intestine disorder, often have severe inflammation and GBA-mediated indirect brain damage. For these reasons, we recommend giving colostrums immediately after delivery and breast milk that has been newly produced throughout the neonatal intensive care unit stay. Ingesting fresh mother's milk encourages the growth of beneficial commensal bacteria in the digestive tract, including probiotic bacteria that thrive on the oligosaccharides found in human milk. Because of this, human breast milk helps babies grow up with fully functional brains and NS. Instead of utilizing a baby formula, neonatal caregivers advocate for the use of donor human milk when a mother is unable to provide her own. The immunomodulatory and antibacterial capabilities of milk proteins are greatly diminished when human donor milk is extensively pasteurized before use. Donor human milk loses some of its antibacterial and immunomodulatory properties after being pasteurized and frozen and thawed. The composition of human milk oligosaccharides differed significantly between donor and maternal milk, suggesting a further investigation into the antimicrobial advantages offered by donor milk.

In light of these studies, we decided to investigate whether or whether the food of extremely low-birth-weight preterm babies affected their risk of developing GBA. To avoid NEC and promote optimum growth and outcomes, nothing beats fresh, pure mother's milk. Friel showed that preterm newborns fed mother's milk fortified at greater than fifty percent had elevated levels of the biomarker urine F2-isoprostane, which indicates oxidant stress. In this study, preterm babies fed either conventional or high-density caloric formulas did not have their urine isoprostanes measured. Researchers found that exposing neutrophils, endothelial, and intestinal epithelial cells assimilate the formula, but not human breast milk, caused cell death in vitro. The study's authors argued that the findings shed light on the causes of NEC. When infants are fed supplemented human milk or cow milk-based formula at a premature stage, they experience a stress response that may interfere with brain development by sending harmful signals through the GBA. Nutritional, microbial, and immunological events linked to brain damage in premature newborns are shown in Figure 4. We underline that these variables may also affect intestinal barrier function, allowing pathogenic microorganisms to invade and translocate, which ultimately results in late-onset newborn sepsis and NEC.

Very premature newborns that were given probiotics had a lower rate of necrotizing enterocolitis. Anti-TNF-alpha and -kappa B pathway inhibitors are produced by probiotic bacteria, according to recent research. Both are inhibited by probiotic bacteria, as was recently discovered. Scientists think probiotics protect the brain by obstructing the GBA, where harmful macromolecules are transported.

Preterm newborns have a threefold increased chance of having ASD, and this remains true even if the most common causes of brain damage in preterm infants—intracranial hemorrhage and ischemia are ruled out. An animal model of autism spectrum disorder was shown to benefit from Bacteroides fragilis therapy by oral administration to progeny. The findings of this study imply that an altered GM contributes to the etiology of ASD. In newborn mice given enteral B. fragilis, an anti-inflammatory milieu (interleukin-10 production) may be the protective strategy.

White matter pathways in the brain are often the site of central NS injuries in premature newborns. Therefore, there is a lot of focus on imaging methods that may characterize connectome damage. Preterm newborns likely suffer brain damage due to harmful substances or neurotransmissions entering the brain through the GBA. Functional magnetic resonance imaging, Magneto, Encephalography, and positron emission tomography are all examples of cutting-edge imaging methods used to probe neural circuits. Researchers will undoubtedly reveal damage instigators connected with the GBA if metagenomic methods are functional toward the GM in tandem with intelligence representation, and the results resolve correspond with human health and illness.

Conclusion.

Because unfavorable environmental impacts may be the origins of ND found in childhood and adulthood, pediatric scientists must concentrate on the gut-brain axis of the fetus or preterm neonate. In this discussion, we have used autism and obesity as examples of GBA-related diseases with developmental origins. Future studies should focus on ND caused by GBA anomalies and try to pin out the underlying processes at work at a young age. Infant feces were collected and studied as part of the Human Microbiome Project. Association with the emergence of autism, cerebral palsy, or other ND in children born with very low birth weights is required to validate the molecular results linked to gut microorganisms in those investigations.

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Conflict of interest statement.

The author declares no conflict of interest.

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