

2019 May 7;15:371-398.

doi: 10.1146/annurev-clinpsy-050718-095432. Epub 2019 Feb 20.

Man and the Microbiome: A New Theory of Everything?

[Mary I Butler](#) ^{1,2}, [John F Cryan](#) ^{2,3}, [Timothy G Dinan](#) ^{1,2}

Affiliations

- PMID: **30786244**
- DOI: [10.1146/annurev-clinpsy-050718-095432](https://doi.org/10.1146/annurev-clinpsy-050718-095432)

Abstract

The gut microbiome is implicated in the pathophysiology of a wide range of psychological disorders. Preclinical studies have provided us with key insights into the mechanisms by which the microbiome influences bidirectional gut-brain communication. There are many signaling pathways involved, including the hypothalamic-pituitary-adrenal axis, immune modulation, tryptophan and serotonin metabolism, bile acid transformation, microbial production of neuroactive compounds, and regulation of the endocannabinoid system. The complex and widespread influence of the microbiome on many physiological and psychological processes has generated a keen interest in its therapeutic potential for depression, anxiety, autism, and other psychiatric disorders. It has been shown that the microbiome composition of people suffering with such conditions differs significantly from that of healthy controls, and although the area is in its infancy, interventional studies that alter a person's microbiome through the use of probiotics, prebiotics, or dietary change can alleviate psychopathological symptoms.

Keywords: anxiety; depression; gut–brain axis; microbiome; microbiota; probiotics.

Similar articles

- [The Gut Microbiome and Mental Health: What Should We Tell Our Patients?: Le microbiote Intestinal et la Santé Mentale : que Devrions-Nous dire à nos Patients?](#) Butler MI, Mörkl S, Sandhu KV, Cryan JF, Dinan TG. *Can J Psychiatry*. 2019 Nov;64(11):747-760. doi: 10.1177/0706743719874168. Epub 2019 Sep 17. PMID: 31530002 Free PMC article. Review.
- [The Microbiota-Gut-Brain Axis in Neuropsychiatric Disorders: Pathophysiological Mechanisms and Novel Treatments.](#) Kim YK, Shin C. *Curr Neuropharmacol*. 2018;16(5):559-573. doi: 10.2174/1570159X15666170915141036. PMID: 28925886 Free PMC article.

- [Gut emotions - mechanisms of action of probiotics as novel therapeutic targets for depression and anxiety disorders.](#) Slyepchenko A, Carvalho AF, Cha DS, Kasper S, McIntyre RS. *CNS Neurol Disord Drug Targets*. 2014;13(10):1770-86. doi: 10.2174/1871527313666141130205242. PMID: 25470391 Review.
- [Harnessing Gut Microbes for Mental Health: Getting From Here to There.](#) Bruce-Keller AJ, Salbaum JM, Berthoud HR. *Biol Psychiatry*. 2018 Feb 1;83(3):214-223. doi: 10.1016/j.biopsych.2017.08.014. Epub 2017 Aug 30. PMID: 29031410 Free PMC article. Review.
- [From isoniazid to psychobiotics: the gut microbiome as a new antidepressant target.](#) Butler MI, Sandhu K, Cryan JF, Dinan TG. *Br J Hosp Med (Lond)*. 2019 Mar 2;80(3):139-145. doi: 10.12968/hmed.2019.80.3.139. PMID: 30860919
- [Modulation of Gut Microbiota-Brain Axis by Probiotics, Prebiotics, and Diet.](#) Liu X, Cao S, Zhang X. *J Agric Food Chem*. 2015 Sep 16;63(36):7885-95. doi: 10.1021/acs.jafc.5b02404. Epub 2015 Sep 1. PMID: 26306709 Review.
- [The "psychomicrobiotic": Targeting microbiota in major psychiatric disorders: A systematic review.](#) Fond G, Boukouaci W, Chevalier G, Regnault A, Eberl G, Hamdani N, Dickerson F, Macgregor A, Boyer L, Dargel A, Oliveira J, Tamouza R, Leboyer M. *Pathol Biol (Paris)*. 2015 Feb;63(1):35-42. doi: 10.1016/j.patbio.2014.10.003. Epub 2014 Nov 2. PMID: 25468489 Review.
- [Impact of gut microbiota on neurological diseases: Diet composition and novel treatments.](#) Larroya-García A, Navas-Carrillo D, Orenes-Piñero E. *Crit Rev Food Sci Nutr*. 2019;59(19):3102-3116. doi: 10.1080/10408398.2018.1484340. Epub 2018 Jul 12. PMID: 29870270 Review.
- [Focus on the essentials: tryptophan metabolism and the microbiome-gut-brain axis.](#) Gheorghe CE, Martin JA, Manriquez FV, Dinan TG, Cryan JF, Clarke G. *Curr Opin Pharmacol*. 2019 Oct;48:137-145. doi: 10.1016/j.coph.2019.08.004. Epub 2019 Oct 14. PMID: 31610413 Review.
- [The role of the microbiome for human health: from basic science to clinical applications.](#) Mohajeri MH, Brummer RJM, Rastall RA, Weersma RK, Harmsen HJM, Faas M, Eggersdorfer M. *Eur J Nutr*. 2018 May;57(Suppl 1):1-14. doi: 10.1007/s00394-018-1703-4. PMID: 29748817 Free PMC article.
- [A gut \(microbiome\) feeling about the brain.](#) Sherwin E, Rea K, Dinan TG, Cryan JF. *Curr Opin Gastroenterol*. 2016 Mar;32(2):96-102. doi: 10.1097/MOG.0000000000000244. PMID: 26760398 Review.
- [Serotonin, tryptophan metabolism and the brain-gut-microbiome axis.](#) O'Mahony SM, Clarke G, Borre YE, Dinan TG, Cryan JF. *Behav Brain Res*. 2015 Jan 15;277:32-48. doi:

10.1016/j.bbr.2014.07.027. Epub 2014 Jul 29. PMID: 25078296 Review.

- [The Gut Microbiome and Mental Health: Implications for Anxiety- and Trauma-Related Disorders.](#) Malan-Muller S, Valles-Colomer M, Raes J, Lowry CA, Seedat S, Hemmings SMJ. OMICS. 2018 Feb;22(2):90-107. doi: 10.1089/omi.2017.0077. Epub 2017 Aug 2. PMID: 28767318 Review.
- [Probiotics and prebiotics: focus on psychiatric disorders - a systematic review.](#) Barbosa RSD, Vieira-Coelho MA. Nutr Rev. 2020 Jun 1;78(6):437-450. doi: 10.1093/nutrit/nuz080. PMID: 31769847
- [Effects of regulating gut microbiota on the serotonin metabolism in the chronic unpredictable mild stress rat model.](#) Li H, Wang P, Huang L, Li P, Zhang D. Neurogastroenterol Motil. 2019 Oct;31(10):e13677. doi: 10.1111/nmo.13677. Epub 2019 Jul 19. PMID: 31323174 Free PMC article.
- [The contribution of the gut microbiome to neurodevelopment and neuropsychiatric disorders.](#) Warner BB. Pediatr Res. 2019 Jan;85(2):216-224. doi: 10.1038/s41390-018-0191-9. Epub 2018 Sep 25. PMID: 30283047 Review.
- [Diet effects in gut microbiome and obesity.](#) Chen J, He X, Huang J. J Food Sci. 2014 Apr;79(4):R442-51. doi: 10.1111/1750-3841.12397. Epub 2014 Mar 12. PMID: 24621052 Review.
- [The Role of Microbiome, Dietary Supplements, and Probiotics in Autism Spectrum Disorder.](#) Sivamaruthi BS, Suganthy N, Kesika P, Chaiyasut C. Int J Environ Res Public Health. 2020 Apr 12;17(8):2647. doi: 10.3390/ijerph17082647. PMID: 32290635 Free PMC article. Review.
- [Targeting gut microbiome: A novel and potential therapy for autism.](#) Yang Y, Tian J, Yang B. Life Sci. 2018 Feb 1;194:111-119. doi: 10.1016/j.lfs.2017.12.027. Epub 2017 Dec 23. PMID: 29277311 Review.
- [Gut Microbiota and the Neuroendocrine System.](#) Farzi A, Fröhlich EE, Holzer P. Neurotherapeutics. 2018 Jan;15(1):5-22. doi: 10.1007/s13311-017-0600-5. PMID: 29380303 Free PMC article. Review.
- [New Therapeutic Drugs from Bioactive Natural Molecules: The Role of Gut Microbiota Metabolism in Neurodegenerative Diseases.](#) Di Meo F, Donato S, Di Pardo A, Maglione V, Filosa S, Crispi S. Curr Drug Metab. 2018;19(6):478-489. doi: 10.2174/1389200219666180404094147. PMID: 29623833 Review.
- [Visceral pain: gut microbiota, a new hope?](#) Pusceddu MM, Gareau MG. J Biomed Sci. 2018 Oct 11;25(1):73. doi: 10.1186/s12929-018-0476-7. PMID: 30309367 Free PMC article. Review.

- [Gut microbiota and health.](#) Kc D, Sumner R, Lippmann S. Postgrad Med. 2020 Apr; 132(3):274. doi: 10.1080/00325481.2019.1662711. Epub 2019 Sep 28. PMID: 31566046 No abstract available.
- [Mind-altering with the gut: Modulation of the gut-brain axis with probiotics.](#) Kim N, Yun M, Oh YJ, Choi HJ. J Microbiol. 2018 Mar;56(3):172-182. doi: 10.1007/s12275-018-8032-4. Epub 2018 Feb 28. PMID: 29492874 Review.
- [Microbiome-Gut-Brain Axis and Toll-Like Receptors in Parkinson's Disease.](#) Caputi V, Giron MC. Int J Mol Sci. 2018 Jun 6;19(6):1689. doi: 10.3390/ijms19061689. PMID: 29882798 Free PMC article. Review.
- [Alcohol, microbiome, and their effect on psychiatric disorders.](#) Hillemacher T, Bachmann O, Kahl KG, Frieling H. Prog Neuropsychopharmacol Biol Psychiatry. 2018 Jul 13;85:105-115. doi: 10.1016/j.pnpbp.2018.04.015. Epub 2018 Apr 26. PMID: 29705711 Review.
- [The Effects of Probiotics and Prebiotics on Mental Disorders: A Review on Depression, Anxiety, Alzheimer, and Autism Spectrum Disorders.](#) Ansari F, Pourjafar H, Tabrizi A, Homayouni A. Curr Pharm Biotechnol. 2020;21(7):555-565. doi: 10.2174/1389201021666200107113812. PMID: 31914909 Review.
- [Can gut microbes play a role in mental disorders and their treatment?](#) Latalova K, Hajda M, Prasko J. Psychiatr Danub. 2017 Mar;29(1):28-30. doi: 10.24869/psyd.2017.28. PMID: 28291971
- [Gut instincts: microbiota as a key regulator of brain development, ageing and neurodegeneration.](#) Dinan TG, Cryan JF. J Physiol. 2017 Jan 15;595(2):489-503. doi: 10.1113/JP273106. Epub 2016 Dec 4. PMID: 27641441 Free PMC article. Review.
- [Gut-Microbiota-Brain Axis and Its Effect on Neuropsychiatric Disorders With Suspected Immune Dysregulation.](#) Petra AI, Panagiotidou S, Hatziagelaki E, Stewart JM, Conti P, Theoharides TC. Clin Ther. 2015 May 1;37(5):984-95. doi: 10.1016/j.clinthera.2015.04.002. PMID: 26046241 Free PMC article. Review.
- [From gut dysbiosis to altered brain function and mental illness: mechanisms and pathways.](#) Rogers GB, Keating DJ, Young RL, Wong ML, Licinio J, Wesselingh S. Mol Psychiatry. 2016 Jun;21(6):738-48. doi: 10.1038/mp.2016.50. Epub 2016 Apr 19. PMID: 27090305 Free PMC article. Review.
- [Fermented foods, the gut and mental health: a mechanistic overview with implications for depression and anxiety.](#) Aslam H, Green J, Jacka FN, Collier F, Berk M, Pasco J, Dawson SL. Nutr Neurosci. 2020 Sep;23(9):659-671. doi: 10.1080/1028415X.2018.1544332. Epub 2018 Nov 11. PMID: 30415609

- [Microbes and mental health: A review.](#) Rieder R, Wisniewski PJ, Alderman BL, Campbell SC. *Brain Behav Immun.* 2017 Nov;66:9-17. doi: 10.1016/j.bbi.2017.01.016. Epub 2017 Jan 25. PMID: 28131791 Review.
- [Gut-Brain Axis and Behavior.](#) Martin CR, Mayer EA. *Nestle Nutr Inst Workshop Ser.* 2017;88:45-53. doi: 10.1159/000461732. Epub 2017 Mar 27. PMID: 28346923 Free PMC article. Review.
- [Exercise-induced stress behavior, gut-microbiota-brain axis and diet: a systematic review for athletes.](#) Clark A, Mach N. *J Int Soc Sports Nutr.* 2016 Nov 24;13:43. doi: 10.1186/s12970-016-0155-6. eCollection 2016. PMID: 27924137 Free PMC article. Review.

[See all similar articles](#)

Cited by 10 articles

- [Role of gut microbiota via the gut-liver-brain axis in digestive diseases.](#) Ding JH, Jin Z, Yang XX, Lou J, Shan WX, Hu YX, Du Q, Liao QS, Xie R, Xu JY. *World J Gastroenterol.* 2020 Oct 28;26(40):6141-6162. doi: 10.3748/wjg.v26.i40.6141. PMID: 33177790 Free PMC article. Review.
- [A Microbial Community Ecology Perspective on the Gut-Microbiome-Brain Axis.](#) van der Goot E, van Spronsen FJ, Falcão Salles J, van der Zee EA. *Front Endocrinol (Lausanne).* 2020 Sep 2;11:611. doi: 10.3389/fendo.2020.00611. eCollection 2020. PMID: 32982988 Free PMC article. No abstract available.
- [Meet Your Stress Management Professionals: The Endocannabinoids.](#) deRoon-Cassini TA, Stollenwerk TM, Beatka M, Hillard CJ. *Trends Mol Med.* 2020 Oct;26(10):953-968. doi: 10.1016/j.molmed.2020.07.002. Epub 2020 Aug 28. PMID: 32868170 Review.
- [Diversity of Gut Microbiota and Bifidobacterial Community of Chinese Subjects of Different Ages and from Different Regions.](#) Yang B, Yan S, Chen Y, Ross RP, Stanton C, Zhao J, Zhang H, Chen W. *Microorganisms.* 2020 Jul 24;8(8):1108. doi: 10.3390/microorganisms8081108. PMID: 32722057 Free PMC article.
- [A Revolutionizing Approach to Autism Spectrum Disorder Using the Microbiome.](#) Johnson D, Letchumanan V, Thurairajasingam S, Lee LH. *Nutrients.* 2020 Jul 3;12(7):1983. doi: 10.3390/nu12071983. PMID: 32635373 Free PMC article. Review.
- [Recipe for a Healthy Gut: Intake of Unpasteurised Milk Is Associated with Increased *Lactobacillus* Abundance in the Human Gut Microbiome.](#) Butler MI, Bastiaanssen TFS, Long-Smith C, Berding K, Morkl S, Cusack AM, Strain C, Busca K, Porteous-Allen P, Claesson MJ, Stanton C, Cryan JF, Allen D, Dinan TG. *Nutrients.* 2020 May 19;12(5):1468. doi: 10.3390/nu12051468. PMID: 32438623 Free PMC article.

- [Mitochondria: An Integrative Hub Coordinating Circadian Rhythms, Metabolism, the Microbiome, and Immunity.](#) Aguilar-López BA, Moreno-Altamirano MMB, Dockrell HM, Duchon MR, Sánchez-García FJ. *Front Cell Dev Biol.* 2020 Feb 7;8:51. doi: 10.3389/fcell.2020.00051. eCollection 2020. PMID: 32117978 Free PMC article. Review.
- [Peripheral Routes to Neurodegeneration: Passing Through the Blood-Brain Barrier.](#) Giannoni P, Claeysen S, Noe F, Marchi N. *Front Aging Neurosci.* 2020 Feb 4;12:3. doi: 10.3389/fnagi.2020.00003. eCollection 2020. PMID: 32116645 Free PMC article. Review.
- [Instrumented Microphysiological Systems for Real-Time Measurement and Manipulation of Cellular Electrochemical Processes.](#) Soucy JR, Bindas AJ, Koppes AN, Koppes RA. *iScience.* 2019 Nov 22;21:521-548. doi: 10.1016/j.isci.2019.10.052. Epub 2019 Oct 28. PMID: 31715497 Free PMC article. Review.
- [Mast Cells in Gut and Brain and Their Potential Role as an Emerging Therapeutic Target for Neural Diseases.](#) Traina G. *Front Cell Neurosci.* 2019 Jul 30;13:345. doi: 10.3389/fncel.2019.00345. eCollection 2019. PMID: 31417365 Free PMC article. Review.