**Supplementary Material**

**Table 3.** Selected Animal Studies Exploring the Role of Gut Biotics on Neurocognitive and Mental Health Conditions

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Condition** | **Study** | **Animal model** | **Gut biotic** | **Outcome** |
| Dementia | Jeong et al, 2015 [224] | Aged Fischer 344 rats | Probiotic: *L. plantarum* KY1032 + *L. curvatus* HY7601 | Mice treated with the probiotic mixture showed improved spatial memory. Rats treated with the probiotic mixture restored age reduced spontaneous alternation in Y-Maze tasks to similar in young rats. |
|  | Liu et al, 2016 [225] | Vascular dementia mouse model | Probiotic: *Clostridium butyrucym* WZMC1016 | Mice treated with the probiotic showed attenuated cognitive dysfunction. In particular decrease escape latency compared to the vascular dementia mice. |
|  | Savignac et al, 2015 [226] | BALB/c mice | Probiotic: *B. longum* 1714 or *B. breve* 1205 | Mice treated with *B. longum* showed improvements in both spatial and non-spatial memory while those treated with *B. breve* only showed improvement in non-spatial memory. |
|  | Gareau et al, 2011 [227] | C57BL/6 mice and GF Swiss-Webster mice | Probiotic: *L. rhamnosus* R0011 + *L. helveticus* R0052 | Mice treated with the probiotic showed improvement in non-spatial memory. |
|  | Davari et al, 2013 [228] | Diabetic rats | Probiotic: *L. acidophilus* 4356 + *B. lactis* 10140 + *L. fermentum* ATCC9338 | Mice treated with probiotics showed reversal of deteriorated brain function, such as cognitive performance. |
|  | Nimgampalle et al, 2017 [143] | Wistar rats treated with D-galactose to induce AD | Probiotic: *L. plantarum* MTCC1325 | The AD group of mice treated with the probiotic showed improved cognition. |
|  | Bonfili et al, 2017 [152] | 3xTg-AD mice | Probiotic: SLAB51 | Probiotic treated mice showed am altered gut microbiota and decreased cognitive decline compared to controls. |
|  | Athari Nik Azm et al, 2018 [229] | Rats injected with β-amyloid | Probiotic: *L. acidophilus, L. fermentum, Bifidobacterium lactis,* and *B. longum* | The AD rats that received the probiotics showed improved spatial memory. |
|  | Abraham et al, 2019 [105] | APP/PS1TG mice  | Probiotic: FRAMELIM- contains *B. longum* and *L. acidophilus* lysates  | Mice subjected to an exercise training and probiotic treatment showed a decreased progression to AD. |
|  | Wang et al, 2020 [230] | APP/PS1TG mice | Probiotic: *L. plantarum* | Probiotic treatment helps remodel the intestinal microbiota and inhibiting the synthesis of TMAO (a gut microbial metabolite that promotes AD progression). |
|  | Kobayashi et al, 2017 [159] | ddY mice | Probiotic: *B. breve* A1Paraprobiotic: *B. breve* A1- heat killedPostbiotic: Sonicated *B. breve A1* and acetate metabolite | The administration of the probiotic in AD mice helped to prevent cognitive dysfunction. They also showed that non-viable components of the bacterium or its metabolite acetate partially ameliorated the cognitive decline in AD mice. |
| Anxiety | Liu et al, 2016 [231] | ELS miceNaive mice | Probiotic: *L. plantarum* PS128 | Naive mice treated with the probiotic showed decreased anxiety-like behaviors while in the ELS mice there was a reduction in depression-like behaviors.  |
| Liu et al, 2016 [232] | GF mice | Probiotic: *L. plantarum* PS128 | GF mice treated with the probiotic showed a decrease in anxiety-like behavior, however, no change in depressive-like behavior. |
|  | Hsiao et al, 2013 [199] | Maternal immune activation mouse model  | Probiotic: *B. fragilis* NCTC9343 | Treatment with the probiotic corrects gut permeability and reduced anxiety-like behavior. |
|  | Wang et al, 2015 [107] | Ampicillin-treated rats | Probiotic: *L. fermentum* NS9 | Probiotic treated rats showed reduced anxiety-like behavior and improved memory retention. |
|  | Smith et al, 2014 [233] | B and T cell-deficient Rag1(-/-) mice | Probiotic: *L. rhamnosus* R0011 + *L. helveticus* R0052 | Rag1(-/-) mice showed increased anxiety and impaired memory which was normalized when treated with the probiotic. |
|  | Luo et al, 2014 [234] | Hyperammonemia induction in Sprague-Dawley rats  | Probiotic: *L. helveticus* R0052 | Rats subjected to the probiotic treatment showed a restoration in cognitive function and improved anxiety-like behavior. |
|  | Savignac et al, 2014 [235] | BALB/c mice | Probiotic: *B. longum* 1714 or *B. breve* 1205 | Mice that were treated with *B. longum* showed a reduction in anxiety-like and depression-like behavior. The mice treated with *B. breve* only showed improvement in anxiety-like behavior. |
|  | Ohland et al, 2013 [236] | IL-10 deficient mice | Probiotic: *L. helveticus* R0052 | There was a reduction in anxiety-like behavior and improvement in memory in mice treated with the probiotic. |
|  | Bercik et al, 2010 [237] | AKR mice infected with Trichuris muris | Probiotic: *B. longum* NCC3001 or *L. rhamnosus* NCC4007 | Mice treated with the probiotic *B. longum* showed reduced anxiety-like behavior. |
|  | Bercik et al, 2011 [238] | Chronic colitis mice model | Probiotic: *B. longum* NCC3001 | Chronic colitis was associated with anxiety-like behavior which was reduced with the administration of the probiotic. |
|  | Messaoudi et al, 2011(a) [239] | Rats | Probiotic: *B. longum* R0175 + *L. helveticus* R0052 | The probiotics taken in combination show significant (P < 0.05) anxiolytic activity in rats. |
|  | Bravo et al, 2011 [240] | Mice | Probiotic: *L. rhamnosus* JB-1 | Treatment with the probiotic reduces stress-induced corticosterone and anxiety-and depression-like behaviors. |
| Depression | Liang et al, 2015 [241] | SPF Sprague-Dawley rats | Probiotic: *L. helveticus* NS8 | Study suggests an anti-depressant effect of the probiotic in rats exposed to chronic restraint stress. Rats showed improved chronic restraint stress-induced behavior (anxiety and depression) and cognitive dysfunction.  |
|  | Desbonnet et al, 2008 [242] | Sprague-Dawley rats | Probiotic: *Bifidobacterium infantis* 35624 | No behavioral change was seen in rats treated with the probiotic. |
|  | Desbonnet et al, 2010 [243] | Maternal separation rat model | Probiotic: *B. infantis* 35624 | Rats treated with the probiotic showed a decrease in depression-like behavior. |
|  | Arseneault-Bread et al, 2012 [244] | Post-MI rats | Probiotic: *B. longum* R0175 + *L. helveticus* R0052 | Post-MI rats displayed less social interaction and depression-like behavior which was reversed with the treatment of probiotics. |
| PTSD | Bharwani et al, 2017 [188] | Male C57BL/6 mice (undergone chronic social defeat) | Probiotic: *L. rhamnosus* JB-1 | Decreased anxiety-like behavior |
| OCD | Kantak et al, 2014 [192] | BALB/cJ house mice | Probiotic: *L. rhamnosus GG* | Treatment with the probiotic attenuated OCD-like behavior and was comparable to fluoxetine treatment |
| Schizophrenia | Hsiao et al, 2013 [199] | MIA mouse model for schizophrenia | Probiotics: *B. fragilis* | Treatment with the probiotic helped reduced anxiety-like, sensorimotor, repetitive and communicative behavior. No change was witnessed in sociability or social preference. |

AD: Alzheimer’s disease; GF: germ-free; ELS: early-life stress; SPF: Specific pathogen free; MI: myocardial infarction; SLAB 51: formulation made of nine live bacterial strains (*Streptococcus thermophilus*, bifidobacteria *(Bifidobacterium longum*, *B. breve*, *B. infantis*), Lactobacilli (*Lactobacillus acidophilus*, *L*. *plantarum*, *L. paracasei*, *L. delbrueckii* subsp. *bulgaricus*, *L. brevis*); TMAO: trimethylamine-N-oxide.

**References**

13. **Morelli L**, Capurso L. FAO/WHO guidelines on probiotics: 10 years later. *J Clin Gastroenterol.* 2012; 46 Suppl:S1-2.

14. **Fijan S**. Microorganisms with claimed probiotic properties: an overview of recent literature*. Int J Environ Res Public Health*. 2014; 11(5): 4745-67.

15. **Min M**, Bunt CR, Mason SL, Hussain MA. Non-dairy probiotic food products: An emerging group of functional foods. *Critical reviews in food science and nutrition* 2019; 59(16): 2626-2641.

16. **Aggarwal N**, Breedon AME, Davis CM, Hwang IY, Chang MW. Engineering probiotics for therapeutic applications: recent examples and translational outlook. *Curr Opin Biotechnol*. 2020; 65: 171-179.

17. **Rijkers GT**, Bengmark S, Enck P, Haller D, Herz U, Kalliomaki M, Kudo S, et. al. Guidance for substantiating the evidence for beneficial effects of probiotics: current status and recommendations for future research. *J Nutr*. 2010; 140(3): 671S-6S.

18. FAO/WHO. Guidelines for the evaluation of probiotics in food. Food Nutr. Pap. 2002. <https://www.who.int/foodsafety/fs_management/en/probiotic_guidelines.pdf>

19. **Lestin F**, Pertschy A, Rimek D. Fungämie nach oraler Gabe von [Fungemia after oral treatment with Saccharomyces boulardii in a patient with multiple comorbidities]. *Dtsch Med Wochenschr*. 2003; 128(48): 2531-3. German.

20. **Santino I**, Alari A, Bono S, Teti E, Marangi M, Bernardini A, Magrini L, et. al. Saccharomyces cerevisiae fungemia, a possible consequence of the treatment of Clostridium difficile colitis with a probioticum. *Int J Immunopathol Pharmacol*. 2014; 27(1): 143-6.

21. **Presterl E**, Kneifel W, Mayer HK, Zehetgruber M, Makristathis A, Graninger W. Endocarditis by Lactobacillus rhamnosus due to yogurt ingestion? *Scand J Infect Dis*. 2001; 33(9): 710-4.

22. **Oggioni MR**, Pozzi G, Valensin PE, Galieni P, Bigazzi C. Recurrent septicemia in an immunocompromised patient due to probiotic strains of Bacillus subtilis. *J Clin Microbiol*. 1998; 36(1): 325-6.

23. **Besselink MG**, Timmerman HM, Buskens E, Nieuwenhuijs VB, Akkermans LM, Gooszen HG; Dutch Acute Pancreatitis Study Group. Probiotic prophylaxis in patients with predicted severe acute pancreatitis (PROPATRIA): design and rationale of a double-blind, placebo-controlled randomised multicenter trial [ISRCTN38327949]. *BMC Surg*. 2004; 4: 12.

24. **Van den Nieuwboer M**, Brummer RJ, Guarner F, Morelli L, Cabana M, Claasen E. The administration of probiotics and synbiotics in immune compromised adults: is it safe? *Benef Microbes*. 2015; 6(1): 3-17.

25. **Didari T**, Solki S, Mozaffari S, Nikfar S, Abdollahi M. A systematic review of the safety of probiotics. *Expert Opin Drug Saf*. 2014 Feb;13(2):227-39.

26. **Hojsak I**, Fabiano V, Pop TL, Goulet O, Zuccotti GV, Çokuğraş FC, Pettoello-Mantovani M, et. al. Guidance on the use of probiotics in clinical practice in children with selected clinical conditions and in specific vulnerable groups. *Acta Paediatr*. 2018; 107(6): 927-937.

27. **Boyle RJ**, Robins-Browne RM, Tang ML. Probiotic use in clinical practice: what are the risks? *Am J Clin Nutr*. 2006; 83(6): 1256-64; quiz 1446-7.

28. **Manzanares W**, Lemieux M, Langlois PL, Wischmeyer PE. Probiotic and synbiotic therapy in critical illness: a systematic review and meta-analysis. *Crit Care*. 2016; 19: 262.

29. **Batra P,** Soni KD, Mathur P. Efficacy of probiotics in the prevention of VAP in critically ill ICU patients: an updated systematic review and meta-analysis of randomized control trials. *J Intensive Care*. 2020; 8: 81.

30. **Fan QL**, Yu XM, Liu QX, Yang W, Chang Q, Zhang YP. Synbiotics for prevention of ventilator-associated pneumonia: a probiotics strain-specific network meta-analysis. *J Int Med Res*. 2019; 47(11): 5349-74.

31. **Gibson GR**, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. *J Nutr*. 1995; 125(6): 1401-12.

32. **Gibson GR**, Scott KP, Rastall RA, Tuohy KM, Hotchkiss A, Dubert-Ferrandon A, Gareau M, Murphy EF, et. al. Dietary prebiotics: Current status and new definition. *IFIS Functional Foods Bulletin* 2010; 7(1): 1-19.

33. **Davani-Davari D**, Negahdaripour M, Karimzadeh I, Seifan M, Mohkam M, Masoumi SJ, Berenjian A, et al. Prebiotics: Definition, Types, Sources, Mechanisms, and *Clinical Applications. Foods*. 2019; 8(3): 92.

34. **Gibson GR**, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, Scott K,et. al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nat Rev Gastroenterol Hepatol.* 2017; 14(8): 491-502.

35. **Pandey KR**, Naik SR, Vakil BV. Probiotics, prebiotics and synbiotics- a review. *J Food Sci Technol.* 2015; 52(12): 7577-87.

36. **Franco-Robles E**, López MG. Implication of fructans in health: immunomodulatory and antioxidant mechanisms. *ScientificWorldJournal*. 2015; 2015: 289267.

37. **Bode L**. Human milk oligosaccharides: prebiotics and beyond. *Nutr Rev*. 2009; 67 Suppl 2: S183-91.

38. **Su P**, Henriksson A, Mitchell H. Prebiotics enhance survival and prolong the retention period of specific probiotic inocula in an in vivo murine model. *J Appl Microbiol*. 2007; 103(6): 2392-400.

39. **Gay-Crosier F**, Schreiber G, Hauser C. Anaphylaxis from inulin in vegetables and processed food. *N Engl J Med*. 2000 May; 342(18): 1372.

40. **Soh JY**, Huang C, Chiang WC, Llanora GV, Lee AJ, Loh W, et al. Anaphylaxis to galacto‐oligosaccharides – an evaluation in an atopic population in Singapore. Allergy (Copenhagen) 2015 Aug;70(8):1020-23.

41. **Bomba A**, Nemcová R, Mudroňová D, Guba P. The possibilities of potentiating the efficacy of probiotics. *Trends in food science & technology* 2002; 13(4): 121-6.

42. **Markowiak P**, Śliżewska K. Effects of Probiotics, Prebiotics, and Synbiotics on Human Health. *Nutrients*. 2017; 9(9): 1021.

43. **Adebola OO**, Corcoran O, Morgan WA. Synbiotics: The impact of potential prebiotics inulin, lactulose and lactobionic acid on the survival and growth of lactobacilli probiotics. *Journal of functional foods* 2014; 10: 75-84.

44. **Bafeta A**, Koh M, Riveros C, Ravaud P. Harms Reporting in Randomized Controlled Trials of Interventions Aimed at Modifying Microbiota: A Systematic Review. *Ann Intern Med.* 2018;169(4): 240-247.

45. **Martín R**, Langella P. Emerging Health Concepts in the Probiotics Field: Streamlining the Definitions*. Front Microbiol*. 2019; 10: 1047.

46**. Barros CP**, Guimarães JT, Esmerino EA, Duarte MCK, Silva MC, Silva R, Ferreira BM, et al. Paraprobiotics and postbiotics: Concepts and potential applications in dairy products. *Current opinion in food science* 2020; 32: 1-8.

47. **Molaee Parvarei M**, Fazeli MR, Mortazavian AM, Sarem Nezhad S, Mortazavi SA, Golabchifar AA, Khorshidian N. Comparative effects of probiotic and paraprobiotic addition on microbiological, biochemical and physical properties of yogurt*. Food research international* 2021; 140: 110030.

48. **Collado MC**, Vinderola G, Salminen S. Postbiotics: facts and open questions. A position paper on the need for a consensus definition. *Benef Microbes*. 2019; 10(7): 711-719.

49. **Aguilar-Toalá** **JE**, Garcia-Varela R, Garcia HS, Mata-Haro V, González-Córdova AF, Vallejo-Cordoba B, Hernández-Mendozaa A. Postbiotics: An evolving term within the functional foods field. *Trends in food science & technology* 2018; 75: 105-114.

50. **de Almada CN**, Almada CN, Martinez RCR, Sant'Ana AS. Paraprobiotics: Evidences on their ability to modify biological responses, inactivation methods and perspectives on their application in foods. *Trends in food science & technology* 2016; 58: 96-114.

51. **Tarsillo B**, Priefer R. Proteobiotics as a new antimicrobial therapy*. Microb Pathog*. 2020; 142: 104093.

52. **Medellin-Peña MJ**, Griffiths MW. Effect of molecules secreted by Lactobacillus acidophilus strain La-5 on Escherichia coli O157:H7 colonization. *Appl Environ Microbiol*. 2009; 75(4): 1165-72.

53. **Klaassen CD**, Cui JY. Review: Mechanisms of How the Intestinal Microbiota Alters the Effects of Drugs and Bile Acids. *Drug Metab Dispos*. 2015; 43(10): 1505-21.

54. **Rouèche E**, Serris E, Thomas G, Périer-Camby L. Influence of temperature on the compaction of an organic powder and the mechanical strength of tablets. Powder technology 2006;162(2):138-144.

55. **Govender M**, Choonara Y, Choonara Y, Kumar P, Kumar P, et al. A review of the advancements in probiotic delivery: Conventional vs. non-conventional formulations for intestinal flora supplementation. AAPS PharmSciTech 2014 Feb;15(1):29-43.

56. **Bolla PA**, de los Angeles Serradell, María, de Urraza PJ, De Antoni GL. Effect of freeze-drying on viability and in vitro probiotic properties of a mixture of lactic acid bacteria and yeasts isolated from kefir. Journal of dairy research 2011 Feb;78(1):15-22.

57. **Bezkorovainy A**. Probiotics: determinants of survival and growth in the gut. Am J Clin Nutr. 2001 Feb;73(2 Suppl):399S-405S.

58. **Marteau P**, Shanahan F. Basic aspects and pharmacology of probiotics: an overview of pharmacokinetics, mechanisms of action and side-effects. *Best Pract Res Clin Gastroenterol*. 2003; 17(5): 725-40.

59. **Cohen LJ**, Esterhazy D, Kim SH, Lemetre C, Aguilar RR, Gordon EA, Pickard AJ, et. al. Commensal bacteria make GPCR ligands that mimic human signalling molecules. *Nature*. 2017; 549(7670): 48-53.

60. **Cryan JF**, Clarke G, Dinan TG, Schellekens H. A Microbial Drugstore for Motility. *Cell Host Microbe*. 2018; 23(6): 691-692.

61. **Stilling RM**, van de Wouw M, Clarke G, Stanton C, Dinan TG, Cryan JF. The neuropharmacology of butyrate: The bread and butter of the microbiota-gut-brain axis? *Neurochem Int*. 2016; 99:110-132.

62. **Lyte M**. Probiotics function mechanistically as delivery vehicles for neuroactive compounds: Microbial endocrinology in the design and use of probiotics. *Bioessays*. 2011; 33(8): 574-81.

63. **Rizkallah MR**, Saad R, Aziz R. The human microbiome project, personalized medicine and the birth of pharmacomicrobiomics. *Current pharmacogenomics and personalized medicine* 2010; 8(3): 182-193.

64. **Haiser HJ**, Turnbaugh PJ. Developing a metagenomic view of xenobiotic metabolism. *Pharmacol Res*. 2013; 69(1): 21-31.

65. **Walsh J**, Griffin BT, Clarke G, Hyland NP. Drug-gut microbiota interactions: implications for neuropharmacology. *Br J Pharmacol*. 2018; 175(24): 4415-4429.

66. **Erickson KL**, Hubbard NE. Probiotic immunomodulation in health and disease. *J Nutr*. 2000; 130(2S Suppl): 403S-409S.

67. **Wu R**, Jeffrey M, Johnson-Henry K, Green-Johnson J, Sherman P. Impact of prebiotics, probiotics and gut derived metabolites on host immunity. *LymphoSign journal* 2016. [[DOI: 10.14785/lymphosign-2016-0012](https://doi.org/10.14785/lymphosign-2016-0012)]

68. **Claassen E**, Van Winsen R, Posno M, Boersma WJ. New and safe "oral" live vaccines based on lactobacillus. Adv Exp Med Biol. 1995; 371B: 1553-8.

69. **Gill HS**. Probiotics to enhance anti-infective defences in the gastrointestinal tract. *Best Pract Res Clin Gastroenterol*. 2003; 17(5): 755-73.

70. **Plaza-Díaz J**, Ruiz-Ojeda FJ, Vilchez-Padial LM, Gil A. Evidence of the Anti-Inflammatory Effects of Probiotics and Synbiotics in Intestinal Chronic Diseases. *Nutrients*. 2017; 9(6): 555.

71. **Goyal D**, Ali SA, Singh RK. Emerging role of gut microbiota in modulation of neuroinflammation and neurodegeneration with emphasis on Alzheimer's disease. *Prog* *Neuropsychopharmacol Biol Psychiatry*. 2021; 106: 110112.

72. **Pluta R**, Ułamek-Kozioł M, Januszewski S, Czuczwar SJ. Gut microbiota and pro/prebiotics in Alzheimer's disease. *Aging* (Albany NY). 2020; 12(6): 5539-5550.

73. **Dimidi E**, Cox SR, Rossi M, Whelan K. Fermented Foods: Definitions and Characteristics, Impact on the Gut Microbiota and Effects on Gastrointestinal Health and Disease. Nutrients. 2019 Aug 5;11(8):1806.

74. **Marco ML**, Heeney D, Binda S, Cifelli CJ, Cotter PD, Foligné B, Gänzle M, et al. Health benefits of fermented foods: microbiota and beyond. Curr Opin Biotechnol. 2017 Apr;44:94-102.

75. **Taylor BC**, Lejzerowicz F, Poirel M, Shaffer JP, Jiang L, Aksenov A, Litwin N, et al. Consumption of Fermented Foods Is Associated with Systematic Differences in the Gut Microbiome and Metabolome. mSystems. 2020 Mar 17;5(2):e00901-19.

76. **Ton AMM**, Campagnaro BP, Alves GA, Aires R, Côco LZ, Arpini CM, et al. Oxidative stress and dementia in alzheimer’s patients: Effects of synbiotic supplementation. Oxidative medicine and cellular longevity 2020 Jan 13,;2020:2638703-14.

77. **Mohammadi AA**, Jazayeri S, Khosravi-Darani K, Solati Z, Mohammadpour N, Asemi Z, Adab Z, et al. The effects of probiotics on mental health and hypothalamic-pituitary-adrenal axis: A randomized, double-blind, placebo-controlled trial in petrochemical workers. Nutr Neurosci. 2016 Nov;19(9):387-395.

78. **Kato-Kataoka A**, Nishida K, Takada M, Kawai M, Kikuchi-Hayakawa H, Suda K, Ishikawa H, et al. Fermented Milk Containing Lactobacillus casei Strain Shirota Preserves the Diversity of the Gut Microbiota and Relieves Abdominal Dysfunction in Healthy Medical Students Exposed to Academic Stress. Appl Environ Microbiol. 2016 May 31;82(12):3649-58.

79. **Aslam H**, Green J, Jacka FN, Collier F, Berk M, Pasco J, Dawson SL. Fermented foods, the gut and mental health: a mechanistic overview with implications for depression and anxiety. Nutr Neurosci. 2020 Sep;23(9):659-671.

80.  **Kobayashi Y**, Kuhara T, Oki M, Xiao JZ. Effects of *Bifidobacterium breve* A1 on the cognitive function of older adults with memory complaints: a randomised, double-blind, placebo-controlled trial. Benef Microbes. 2019 May 28;10(5):511-520.

81. **Xiao J**, Katsumata N, Bernier F, Ohno K, Yamauchi Y, Odamaki T, et al. Probiotic Bifidobacterium breve in Improving Cognitive Functions of Older Adults with Suspected Mild Cognitive Impairment: A Randomized, Double-Blind, Placebo-Controlled Trial. J Alzheimers Dis. 2020;77(1):139-147.

82. **Hwang YH**, Park S, Paik JW, Chae SW, Kim DH, Jeong DG, Ha E, et al. Efficacy and Safety of *Lactobacillus Plantarum* C29-Fermented Soybean (DW2009) in Individuals with Mild Cognitive Impairment: A 12-Week, Multi-Center, Randomized, Double-Blind, Placebo-Controlled Clinical Trial. Nutrients. 2019 Feb 1;11(2):305.

83. **Akbari E**, Asemi Z, Daneshvar Kakhaki R, Bahmani F, Kouchaki E, Tamtaji OR, Hamidi GA, et. al. Effect of Probiotic Supplementation on Cognitive Function and Metabolic Status in Alzheimer's Disease: A Randomized, Double-Blind and Controlled Trial. *Front Aging Neurosci.* 2016; 8: 256.

84. **Tamtaji OR**, Heidari-Soureshjani R, Mirhosseini N, Kouchaki E, Bahmani F, Aghadavod E, Tajabadi-Ebrahimi M, Asemi Z. Probiotic and selenium co-supplementation, and the effects on clinical, metabolic and genetic status in Alzheimer's disease: A randomized, double-blind, controlled trial. Clin Nutr. 2019 Dec;38(6):2569-2575.

85. **Den H**, Dong X, Chen M, Zou Z. Efficacy of probiotics on cognition, and biomarkers of inflammation and oxidative stress in adults with Alzheimer's disease or mild cognitive impairment - a meta-analysis of randomized controlled trials. Aging (Albany NY). 2020 Feb 15;12(4):4010-4039.

86. **Lv T**, Ye M, Luo F, Hu B, Wang A, Chen J, Yan J, et al. Probiotics treatment improves cognitive impairment in patients and animals: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2021 Jan;120:159-172.

87.  **Otaka M**, Kikuchi-Hayakawa H, Ogura J, Ishikawa H, Yomogida Y, Ota M, et al. Effect of lacticaseibacillus paracasei strain shirota on improvement in depressive symptoms, and its association with abundance of actinobacteria in gut microbiota. Microorganisms (Basel) 2021 May 10,;9(5):1026.

88. **Akkasheh G**, Kashani-Poor Z, Tajabadi-Ebrahimi M, Jafari P, Akbari H, Taghizadeh M, Memarzadeh MR, et al. Clinical and metabolic response to probiotic administration in patients with major depressive disorder: A randomized, double-blind, placebo-controlled trial. Nutrition. 2016 Mar;32(3):315-20.

89. **Kazemi A**, Noorbala AA, Azam K, Eskandari MH, Djafarian K. Effect of probiotic and prebiotic vs placebo on psychological outcomes in patients with major depressive disorder: A randomized clinical trial. Clin Nutr. 2019 Apr;38(2):522-528.

90. **Eskandarzadeh S**, Effatpanah M, Khosravi-Darani K, Askari R, Hosseini AF, Reisian M, Jazayeri S. Efficacy of a multispecies probiotic as adjunctive therapy in generalized anxiety disorder: a double blind, randomized, placebo-controlled trial. Nutr Neurosci. 2021 Feb;24(2):102-108.

91. **Shvachko NA**, Loskutov IG, Semilet TV, Popov VS, Kovaleva ON, Konarev AV. Bioactive components in oat and barley grain as a promising breeding trend for functional food production. Molecules (Basel, Switzerland) 2021 Apr 14,;26(8):2260.

92. **Kennedy DO**, Bonnländer B, Lang SC, Pischel I, Forster J, Khan J, et al. Acute and chronic effects of green oat ( avena sativa) extract on cognitive function and mood during a laboratory stressor in healthy adults: A randomised, double-blind, placebo-controlled study in healthy humans. Nutrients 2020 May 29,;12(6):1598.

93. **Alhassani W**. The Effects of a High Fiber Beta Glucan Talbina Meal on Emotional Well-being Among Syrian Refugees in Metropolitan Detroit (P08-076-19). Curr Dev Nutr. 2019 Oct 24;3(Suppl 1):nzz044.P08-076-19.

94. **Mottaghi T**, Amirabdollahian F, Haghighatdoost F. Fruit and vegetable intake and cognitive impairment: a systematic review and meta-analysis of observational studies. Eur J Clin Nutr. 2018 Oct;72(10):1336-1344.

95**. Nurk E**, Refsum H, Drevon CA, Tell GS, Nygaard HA, Engedal K, Smith AD. Cognitive performance among the elderly in relation to the intake of plant foods. The Hordaland Health Study. Br J Nutr. 2010 Oct;104(8):1190-201.

96. **Gehlich KH**, Beller J, Lange-Asschenfeldt B, Köcher W, Meinke MC, Lademann J. Fruit and vegetable consumption is associated with improved mental and cognitive health in older adults from non-western developing countries. Public health nutrition 2019 Mar;22(4):689-696.

97. **Kim CS**, Byeon S, Shin DM. Sources of Dietary Fiber Are Differently Associated with Prevalence of Depression. Nutrients. 2020 Sep 14;12(9):2813. doi: 10.3390/nu12092813. PMID: 32937844; PMCID: PMC7551178.

98. **Xu H**, Li S, Song X, Li Z, Zhang D. Exploration of the association between dietary fiber intake and depressive symptoms in adults. Nutrition. 2018 Oct;54:48-53.

99. **Matison AP**, Mather KA, Flood VM, Reppermund S. Associations between nutrition and the incidence of depression in middle-aged and older adults: A systematic review and meta-analysis of prospective observational population-based studies. Ageing Res Rev. 2021 Sep;70:101403.

100. **Desmedt O**, Broers VJV, Zamariola G, Pachikian B, Delzenne N, Luminet O. Effects of prebiotics on affect and cognition in human intervention studies. Nutr Rev. 2019 Feb 1;77(2):81-95.

101. **Smith AP**, Sutherland D, Hewlett P. An Investigation of the Acute Effects of Oligofructose-Enriched Inulin on Subjective Wellbeing, Mood and Cognitive Performance. Nutrients. 2015 Oct 28;7(11):8887-96.

102. **Marx W**, Scholey A, Firth J, D’Cunha NM, Lane M, Hockey M, et al. Prebiotics, probiotics, fermented foods and cognitive outcomes: A meta-analysis of randomized controlled trials. Neuroscience and biobehavioral reviews 2020 Nov;118:472-484.

103. **Halverson T**, Alagiakrishnan K. Gut microbes in neurocognitive and mental health disorders. *Ann Med*. 2020; 52(8): 423-443.

104. **Hort J**, Valis M, Angelucci F. Administration of pre/probiotics with conventional drug treatment in Alzheimer's disease. *Neural Regen Res*. 2020; 15(3): 448-449.

105. **Abraham D**, Feher J, Scuderi GL, Szabo D, Dobolyi A, Cservenak M, Juhasz J, et. al. Exercise and probiotics attenuate the development of Alzheimer's disease in transgenic mice: Role of microbiome. *Exp Gerontol*. 2019; 115: 122-131.

106. **Neufeld KA**, Kang N, Bienenstock J, Foster JA. Effects of intestinal microbiota on anxiety-like behavior. *Commun Integr Biol*. 2011; 4(4): 492-4.

107. **Wang T**, Hu X, Liang S, Li W, Wu X, Wang L, Jin F. Lactobacillus fermentum NS9 restores the antibiotic induced physiological and psychological abnormalities in rats. *Benef Microbes*. 2015; 6(5): 707-17.

108. **Pistollato F**, Iglesias RC, Ruiz R, Aparicio S, Crespo J, Lopez LD, Manna PP, et. al. Nutritional patterns associated with the maintenance of neurocognitive functions and the risk of dementia and Alzheimer's disease: A focus on human studies. *Pharmacol Res*. 2018; 131: 32-43.

109. **Lukić I**, Getselter D, Ziv O, Oron O, Reuveni E, Koren O, Elliott E. Antidepressants affect gut microbiota and Ruminococcus flavefaciens is able to abolish their effects on depressive-like behavior. *Transl Psychiatry*. 2019; 9(1): 133.

110. **Kao AC**, Spitzer S, Anthony DC, Lennox B, Burnet PWJ. Prebiotic attenuation of olanzapine-induced weight gain in rats: analysis of central and peripheral biomarkers and gut microbiota. *Transl Psychiatry*. 2018; 8(1): 66.

111. **Lianov L**, Johnson M. Physician competencies for prescribing lifestyle medicine. JAMA. 2010 Jul 14;304(2):202-3.

112. **Firth J**, Solmi M, Wootton RE, Vancampfort D, Schuch FB, Hoare E, Gilbody S, et al. A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders. World Psychiatry. 2020 Oct;19(3):360-380.

113. **Savin Z**, Kivity S, Yonath H, Yehuda S. Smoking and the intestinal microbiome. Arch Microbiol. 2018 Jul;200(5):677-684.

114. **Gui X**, Yang Z, Li MD. Effect of Cigarette Smoke on Gut Microbiota: State of Knowledge. Front Physiol. 2021 Jun 17;12:673341.

115. **Lee SH**, Yun Y, Kim SJ, Lee EJ, Chang Y, Ryu S, Shin H, et al. Association between Cigarette Smoking Status and Composition of Gut Microbiota: Population-Based Cross-Sectional Study. J Clin Med. 2018 Sep 14;7(9):282.

116. **Sublette MG**, Cross TL, Korcarz CE, Hansen KM, Murga-Garrido SM, Hazen SL, et al. Effects of smoking and smoking cessation on the intestinal microbiota. Journal of clinical medicine 2020 Sep 14,;9(9):2963.

117. **Biedermann L**, Zeitz J, Mwinyi J, Sutter-Minder E, Rehman A, Ott SJ, Steurer-Stey C, et al. Smoking cessation induces profound changes in the composition of the intestinal microbiota in humans. PLoS One. 2013;8(3):e59260.

118. **Ames NJ**, Barb JJ, Schuebel K, Mudra S, Meeks BK, Tuason RTS, Brooks AT, et al. Longitudinal gut microbiome changes in alcohol use disorder are influenced by abstinence and drinking quantity. Gut Microbes. 2020 Nov 1;11(6):1608-1631.

119. **Stefanaki C**, Mastorakos G, Chrousos GP. Gut microbiome and mental stress-related disorders: The interplay of classic and microbial endocrinology. Gut microbiome-related diseases and therapies Cham: Springer International Publishing; 2021. p. 229-242.

120. **Wu SI**, Wu CC, Tsai PJ, Cheng LH, Hsu CC, Shan IK, Chan PY, et al. Psychobiotic Supplementation of PS128TM Improves Stress, Anxiety, and Insomnia in Highly Stressed Information Technology Specialists: A Pilot Study. Front Nutr. 2021 Mar 26;8:614105.

121. **Smith RP**, Easson C, Lyle SM, Kapoor R, Donnelly CP, Davidson EJ, Parikh E, et al. Gut microbiome diversity is associated with sleep physiology in humans. PLoS One. 2019 Oct 7;14(10):e0222394.

122. **Irwin C**, McCartney D, Desbrow B, Khalesi S. Effects of probiotics and paraprobiotics on subjective and objective sleep metrics: A systematic review and meta-analysis. European journal of clinical nutrition 2020 Nov;74(11):1536-1549.

123. **Clauss M**, Gérard P, Mosca A, Leclerc M. Interplay Between Exercise and Gut Microbiome in the Context of Human Health and Performance. Front Nutr. 2021 Jun 10;8:637010. doi: 10.3389/fnut.2021.637010.

124. **Sánchez-Villegas A**, Toledo E, de Irala J, Ruiz-Canela M, Pla-Vidal J, Martínez-González MA. Fast-food and commercial baked goods consumption and the risk of depression. Public Health Nutr. 2012 Mar;15(3):424-32.

125. **Hu D**, Cheng L, Jiang W. Sugar-sweetened beverages consumption and the risk of depression: A meta-analysis of observational studies. J Affect Disord. 2019 Feb 15;245:348-355.

126. **Zhu C**, Sawrey-Kubicek L, Beals E, Rhodes CH, Houts HE, Sacchi R, Zivkovic AM. Human gut microbiome composition and tryptophan metabolites were changed differently by fast food and Mediterranean diet in 4 days: a pilot study. Nutr Res. 2020 May;77:62-72.

127. **Spierling SR**, Zorrilla EP. Don't stress about CRF: assessing the translational failures of CRF1antagonists*. Psychopharmacology* (Berl). 2017; 234(9-10): 1467-1481.

128. **Hoffmann DE**, Fraser CM, Palumbo F, Ravel J, Rowthorn V, Schwartz J. Probiotics: achieving a better regulatory fit. *Food Drug Law J*. 2014; 69(2): 237-72.

129. **Chinna Meyyappan A**, Forth E, Wallace CJK, Milev R. Effect of fecal microbiota transplant on symptoms of psychiatric disorders: a systematic review. *BMC Psychiatry*. 2020 Jun 15;20(1):299.

130. **D'Amato A**, Di Cesare Mannelli L, Lucarini E, Man AL, Le Gall G, Branca JJV, Ghelardini C, et. al. Faecal microbiota transplant from aged donor mice affects spatial learning and memory via modulating hippocampal synaptic plasticity- and neurotransmission-related proteins in young recipients. *Microbiome*. 2020; 8(1): 140.

131. **Sun J**, Xu J, Ling Y, Wang F, Gong T, Yang C, Ye S, et. al. Fecal microbiota transplantation alleviated Alzheimer's disease-like pathogenesis in APP/PS1 transgenic mice*. Transl Psychiatry*. 2019; 9(1): 189.

132. **Hazan S**. Rapid improvement in Alzheimer's disease symptoms following fecal microbiota transplantation: a case report. *J Int Med Res*. 2020; 48(6): 300060520925930.

133. **Zhang Y**, Huang R, Cheng M, Wang L, Chao J, Li J, Zheng P, et. al. Gut microbiota from NLRP3-deficient mice ameliorates depressive-like behaviors by regulating astrocyte dysfunction via circHIPK2. *Microbiome*. 2019; 7(1): 116.

134. **Liu S**, Guo R, Liu F, Yuan Q, Yu Ren F. Gut Microbiota Regulates Depression-Like Behavior in Rats Through the Neuroendocrine-Immune-Mitochondrial Pathway. *Neuropsychiatr Dis Treat*. 2020; 16: 859-869.

135. **De Palma G**, Lynch MD, Lu J, Dang VT, Deng Y, Jury J, Umeh G, et. al. Transplantation of fecal microbiota from patients with irritable bowel syndrome alters gut function and behavior in recipient mice. *Sci Transl Med*. 2017; 9(379): eaaf6397.

136. **Huang HL**, Chen HT, Luo QL, Xu HM, He J, Li YQ, Zhou YL, et. al. Relief of irritable bowel syndrome by fecal microbiota transplantation is associated with changes in diversity and composition of the gut microbiota*. J Dig Dis*. 2019; 20(8): 401-408.

137. **Cai T**, Shi X, Yuan LZ, Tang D, Wang F. Fecal microbiota transplantation in an elderly patient with mental depression. *Int Psychogeriatr*. 2019; 31(10): 1525-1526.

138. **Köhler CA**, Maes M, Slyepchenko A, Berk M, Solmi M, Lanctôt KL, Carvalho AF. The Gut-Brain Axis, Including the Microbiome, Leaky Gut and Bacterial Translocation: Mechanisms and Pathophysiological Role in Alzheimer's Disease. *Curr Pharm Des*. 2016; 22(40): 6152-6166.

139. **Li B**, He Y, Ma J, Huang P, Du J, Cao L, Wang Y, et. al. Mild cognitive impairment has similar alterations as Alzheimer's disease in gut microbiota. *Alzheimers Dement*. 2019; 15(10): 1357-1366.

140. **Sachdev PS**, Lipnicki DM, Crawford J, Reppermund S, Kochan NA, Trollor JN, Draper B, et. al. Risk profiles for mild cognitive impairment vary by age and sex: the Sydney Memory and Ageing study. *Am J Geriatr Psychiatry*. 2012; 20(10): 854-65.

141. **Tokuchi R**, Hishikawa N, Kurata T, Sato K, Kono S, Yamashita T, Deguchi K, et. al. Clinical and demographic predictors of mild cognitive impairment for converting to Alzheimer's disease and reverting to normal cognition. *J Neurol Sci*. 2014; 346(1-2): 288-92.

142. **Prince M**, Ali GC, Guerchet M, Prina AM, Albanese E, Wu YT. Recent global trends in the prevalence and incidence of dementia, and survival with dementia. *Alzheimers Res Ther*. 2016; 8(1): 23.

143. **Nimgampalle M**, Kuna Y. Anti-Alzheimer Properties of Probiotic, *Lactobacillus plantarum* MTCC 1325 in Alzheimer's Disease induced Albino Rats. *J Clin Diagn Res*. 2017 Aug;11(8): KC01-KC05.

144. **Angelucci F**, Cechova K, Amlerova J, Hort J. Antibiotics, gut microbiota, and Alzheimer's disease. *J Neuroinflammation*. 2019; 16(1): 108.

145**. McDaniel MA**, Maier SF, Einstein GO. "Brain-specific" nutrients: a memory cure? *Nutrition*. 2003; 19(11-12): 957-75.

146. **Dos Santos Guilherme M**, Todorov H, Osterhof C, Möllerke A, Cub K, Hankeln T, Gerber S, et. al. Impact of Acute and Chronic Amyloid-β Peptide Exposure on Gut Microbial Commensals in the Mouse. *Front Microbiol*. 2020; 11: 1008.

147. **Fujii Y**, Nguyen TTT, Fujimura Y, Kameya N, Nakamura S, Arakawa K, Morita H. Fecal metabolite of a gnotobiotic mouse transplanted with gut microbiota from a patient with Alzheimer's disease. *Biosci Biotechnol Biochem*. 2019; 83(11): 2144-2152.

148**. Zhao Y**, Lukiw WJ. Microbiome-generated amyloid and potential impact on amyloidogenesis in Alzheimer's disease (AD). *J Nat Sci*. 2015; 1(7): e138.

149. **Prinz M**, Priller J. Microglia and brain macrophages in the molecular age: from origin to neuropsychiatric disease. *Nat Rev Neurosci*. 2014; 15(5): 300-12.

150. **Erny D**, Hrabě de Angelis AL, Jaitin D, Wieghofer P, Staszewski O, David E, Keren-Shaul H, et. al. Host microbiota constantly control maturation and function of microglia in the CNS*. Nat Neurosci*. 2015; 18(7): 965-77.

151. **Mancuso C**, Santangelo R. Alzheimer's disease and gut microbiota modifications: The long way between preclinical studies and clinical evidence. *Pharmacol Res*. 2018; 129: 329-336.

152. **Bonfili L**, Cecarini V, Berardi S, Scarpona S, Suchodolski JS, Nasuti C, Fiorini D, et. al. Microbiota modulation counteracts Alzheimer's disease progression influencing neuronal proteolysis and gut hormones plasma levels. *Sci Rep*. 2017; 7(1): 2426.

153. **Wang H**, Lee IS, Braun C, Enck P. Effect of Probiotics on Central Nervous System Functions in Animals and Humans: A Systematic Review. *J Neurogastroenterol Motil*. 2016; 22(4): 589-605.

154**. Tsai YL**, Lin TL, Chang CJ, Wu TR, Lai WF, Lu CC, Lai HC. Probiotics, prebiotics and amelioration of diseases. J Biomed Sci. 2019; 26(1): 3.

155**. Larroya-García A**, Navas-Carrillo D, Orenes-Piñero E. Impact of gut microbiota on neurological diseases: Diet composition and novel treatments. *Crit Rev Food Sci Nutr*. 2019; 59(19): 3102-3116.

156. **Wang X**, Liu GJ, Gao Q, Li N, Wang RT. C-type lectin-like receptor 2 and zonulin are associated with mild cognitive impairment and Alzheimer's disease. *Acta Neurol Scand*. 2020; 141(3): 250-255.

157. **Tillisch K**, Labus J, Kilpatrick L, Jiang Z, Stains J, Ebrat B, Guyonnet D, et. al. Consumption of fermented milk product with probiotic modulates brain activity. *Gastroenterology*. 2013; 144(7): 1394-401, 1401.e1-4.

158. **Saji N**, Niida S, Murotani K, Hisada T, Tsuduki T, Sugimoto T, Kimura A, et. al. Analysis of the relationship between the gut microbiome and dementia: a cross-sectional study conducted in Japan. *Sci Rep*. 2019; 9(1): 1008.

159. **Kobayashi Y**, Sugahara H, Shimada K, Mitsuyama E, Kuhara T, Yasuoka A, Kondo T, et. al. Therapeutic potential of Bifidobacterium breve strain A1 for preventing cognitive impairment in Alzheimer's disease. *Sci Rep*. 2017; 7(1): 13510.

160. **Łuc M**, Misiak B, Pawłowski M, Stańczykiewicz B, Zabłocka A, Szcześniak D, Pałęga A, et. al. Gut microbiota in dementia. Critical review of novel findings and their potential application. *Prog Neuropsychopharmacol Biol Psychiatry*. 2021; 104: 110039.

161. **Krüger JF**, Hillesheim E, Pereira ACSN, Camargo CQ, Rabito EI. Probiotics for dementia: a systematic review and meta-analysis of randomized controlled trials. *Nutr R*ev. 2021; 79(2): 160-170.

162. **Sochocka M**, Donskow-Łysoniewska K, Diniz BS, Kurpas D, Brzozowska E, Leszek J. The Gut Microbiome Alterations and Inflammation-Driven Pathogenesis of Alzheimer's Disease-a Critical Review. *Mol Neurobiol*. 2019; 56(3): 1841-1851.

163. **Cattaneo A**, Cattane N, Galluzzi S, Provasi S, Lopizzo N, Festari C, Ferrari C, et. al. Association of brain amyloidosis with pro-inflammatory gut bacterial taxa and peripheral inflammation markers in cognitively impaired elderly. *Neurobiol Aging*. 2017; 49:60-68.

164. **Jiang C**, Li G, Huang P, Liu Z, Zhao B. The Gut Microbiota and Alzheimer's Disease. *J Alzheimers Dis*. 2017; 58(1): 1-15.

165. **Kao AC**, Harty S, Burnet PW. The Influence of Prebiotics on Neurobiology and Behavior. *Int Rev Neurobiol*. 2016; 131: 21-48.

166. **Serra MC**, Nocera JR, Kelleher JL, Addison O. Prebiotic Intake in Older Adults: Effects on Brain Function and Behavior. *Curr Nutr Rep*. 2019; 8(2): 66-73.

167. **Chen D**, Yang X, Yang J, Lai G, Yong T, Tang X, Shuai O, et. al. Prebiotic Effect of Fructooligosaccharides from *Morinda officinalis* on Alzheimer's Disease in Rodent Models by Targeting the Microbiota-Gut-Brain Axis. *Front Aging Neurosci*. 2017; 9: 403.

168. **Sun J**, Liu S, Ling Z, Wang F, Ling Y, Gong T, Fang N, et. al. Fructooligosaccharides Ameliorating Cognitive Deficits and Neurodegeneration in APP/PS1 Transgenic Mice through Modulating Gut Microbiota. *J Agric Food Chem*. 2019; 67(10): 3006-3017.

169. **Hoffman JD**, Yanckello LM, Chlipala G, Hammond TC, McCulloch SD, Parikh I, Sun S, et. al. Dietary inulin alters the gut microbiome, enhances systemic metabolism and reduces neuroinflammation in an APOE4 mouse model. *PLoS One*. 2019; 14(8): e0221828.

170. **Jia S**, Lu Z, Gao Z, An J, Wu X, Li X, Dai X, et. al. Chitosan oligosaccharides alleviate cognitive deficits in an amyloid-β1-42-induced rat model of Alzheimer's disease*. Int J Biol Macromol*. 2016; 83: 416-25.

171. **Prasad S**, Dhiman RK, Duseja A, Chawla YK, Sharma A, Agarwal R. Lactulose improves cognitive functions and health-related quality of life in patients with cirrhosis who have minimal hepatic encephalopathy. *Hepatology*. 2007; 45(3): 549-59.

172. **Romo-Araiza A**, Gutiérrez-Salmeán G, Galván EJ, Hernández-Frausto M, Herrera-López G, Romo-Parra H, García-Contreras V, et. al. Probiotics and Prebiotics as a Therapeutic Strategy to Improve Memory in a Model of Middle-Aged Rats. *Front Aging Neurosci*. 2018; 10: 416.

173. **Louzada ER**, Ribeiro SML. Synbiotic supplementation, systemic inflammation, and symptoms of brain disorders in elders: A secondary study from a randomized clinical trial. *Nutr Neurosci*. 2020; 23(2): 93-100.

174. **Wang PX**, Deng XR, Zhang CH, Yuan HJ. Gut microbiota and metabolic syndrome. *Chin Med J (Engl).* 2020; 133(7): 808-816.

175. **Yu JY**, Zhang B, Peng L, Wu CH, Cao H, Zhong JF, Hoffman J, et. al. Repositioning of Memantine as a Potential Novel Therapeutic Agent against Meningitic E. coli-Induced Pathogenicities through Disease-Associated Alpha7 Cholinergic Pathway and RNA Sequencing-Based Transcriptome Analysis of Host Inflammatory Responses. *PLoS One*. 2015; 10(5): e0121911.

176. **James SL**, Geleijnse JM. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: A systematic analysis for the global burden of disease study 2017. The Lancet (British edition) 2018;392(10159):1789-1858.

177. **McVey Neufeld KA**, O'Mahony SM, Hoban AE, Waworuntu RV, Berg BM, Dinan TG, Cryan JF. Neurobehavioural effects of Lactobacillus rhamnosus GG alone and in combination with prebiotics polydextrose and galactooligosaccharide in male rats exposed to early-life stress. *Nutr Neurosci.* 2019; 22(6): 425-434.

178. **Szklany K**, Wopereis H, de Waard C, van Wageningen T, An R, van Limpt K, Knol J, et. al. Supplementation of dietary non-digestible oligosaccharides from birth onwards improve social and reduce anxiety-like behaviour in male BALB/c mice. *Nutr Neurosci*. 2020; 23(11): 896-910.

179. **Mika A**, Gaffney M, Roller R, Hills A, Bouchet CA, Hulen KA, Thompson RS, et. al. Feeding the developing brain: Juvenile rats fed diet rich in prebiotics and bioactive milk fractions exhibit reduced anxiety-related behavior and modified gene expression in emotion circuits. *Neurosci Lett*. 2018; 677: 103-109.

180. **Schmidt K**, Cowen PJ, Harmer CJ, Tzortzis G, Errington S, Burnet PW. Prebiotic intake reduces the waking cortisol response and alters emotional bias in healthy volunteers. *Psychopharmacology (Berl)*. 2015; 232(10): 1793-801.

181. **Ghorbani Z**, Nazari S, Etesam F, Nourimajd S, Ahmadpanah M, Razeghi Jahromi S. The effect of synbiotic as an adjuvant therapy to fluoxetine in moderate depression: A randomized multicenter trial. *Archives of neuroscience* 2018; 5(2) [DOI: [10.5812/archneurosci.60507](https://dx.doi.org/10.5812/archneurosci.60507)]

182. **Silk DB**, Davis A, Vulevic J, Tzortzis G, Gibson GR. Clinical trial: the effects of a trans-galactooligosaccharide prebiotic on faecal microbiota and symptoms in irritable bowel syndrome. *Aliment Pharmacol Ther*. 2009; 29(5): 508-18.

183. **Azpiroz F**, Dubray C, Bernalier-Donadille A, Cardot JM, Accarino A, Serra J, Wagner A, et. al. Effects of scFOS on the composition of fecal microbiota and anxiety in patients with irritable bowel syndrome: a randomized, double blind, placebo-controlled study. *Neurogastroenterol Motil*. 2017; 29(2).

184. **Talbott SM**, Talbott JA. Baker's yeast beta-glucan supplement reduces upper respiratory symptoms and improves mood state in stressed women. *J Am Coll Nutr*. 2012; 31(4): 295-300.

185. **Gruenwald J**, Graubaum HJ, Harde A. Effect of a probiotic multivitamin compound on stress and exhaustion. *Adv Ther*. 2002; 19(3): 141-50.

186. **Diop L**, Guillou S, Durand H. Probiotic food supplement reduces stress-induced gastrointestinal symptoms in volunteers: a double-blind, placebo-controlled, randomized trial. *Nutr Res*. 2008; 28(1): 1-5.

187. **Yang H**, Zhao X, Tang S, Huang H, Zhao X, Ning Z, Fu X, et. al. Probiotics reduce psychological stress in patients before laryngeal cancer surgery. *Asia Pac J Clin Oncol*. 2016; 12(1): e92-6.

188. **Bharwani A**, Mian MF, Surette MG, Bienenstock J, Forsythe P. Oral treatment with Lactobacillus rhamnosus attenuates behavioural deficits and immune changes in chronic social stress. *BMC Med*. 2017; 15(1): 7.

189. **Liu Y**, Steinhausen K, Bharwani A, Mian MF, McVey Neufeld KA, Forsythe P. Increased persistence of avoidance behaviour and social deficits with L.rhamnosus JB-1 or selective serotonin reuptake inhibitor treatment following social defeat. *Sci Rep*. 2020; 10(1): 13485.

190. **Gocan AG**, Bachg D, Schindler AE, Rohr UD. Balancing steroidal hormone cascade in treatment-resistant veteran soldiers with PTSD using a fermented soy product (FSWW08): a pilot study. *Horm Mol Biol Clin Investig*. 2012; 10(3): 301-14.

191. American Psychiatric Association. (2013) Diagnostic and statistical manual of mental disorders (5th ed). Arlington, VA: American Psychiatric Association

192. **Kantak PA**, Bobrow DN, Nyby JG. Obsessive-compulsive-like behaviors in house mice are attenuated by a probiotic (Lactobacillus rhamnosus GG). *Behav Pharmacol*. 2014; 25(1): 71-9.

193. **Sanikhani NS**, Modarressi MH, Jafari P, Vousooghi N, Shafei S, Akbariqomi M, et al. The effect of lactobacillus casei consumption in improvement of obsessive-compulsive disorder: An animal study. Probiotics Antimicrob Proteins. 2020;12(4):1409-1419.

194. **Messaoudi M**, Violle N, Bisson JF, Desor D, Javelot H, Rougeot C. Beneficial psychological effects of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in healthy human volunteers. *Gut Microbes*. 2011; 2(4): 256-61.

195. **Zheng P**, Zeng B, Liu M, Chen J, Pan J, Han Y, Liu Y, et. al. The gut microbiome from patients with schizophrenia modulates the glutamate-glutamine-GABA cycle and schizophrenia-relevant behaviors in mice. *Sci Adv*. 2019; 5(2): eaau8317.

196. **Schwarz E**, Maukonen J, Hyytiäinen T, Kieseppä T, Orešič M, Sabunciyan S, Mantere O, et. al. Analysis of microbiota in first episode psychosis identifies preliminary associations with symptom severity and treatment response. *Schizophr Res*. 2018; 192: 398-403.

197. **Naidu AS**, Bidlack WR, Clemens RA. Probiotic spectra of lactic acid bacteria (LAB). *Crit Rev Food Sci Nutr*. 1999; 39(1): 13-126.

198. **Olde Loohuis LM**, Mangul S, Ori APS, Jospin G, Koslicki D, Yang HT, Wu T, et. al. Transcriptome analysis in whole blood reveals increased microbial diversity in schizophrenia. *Transl Psychiatry*. 2018 May; 8(1): 96.

199. **Hsiao EY**, McBride SW, Hsien S, Sharon G, Hyde ER, McCue T, Codelli JA, et. al. Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. *Cell*. 2013; 155(7): 1451-63.

200. **De Hert M**, Dockx L, Bernagie C, Peuskens B, Sweers K, Leucht S, Tack J, et. al. Prevalence and severity of antipsychotic related constipation in patients with schizophrenia: a retrospective descriptive study. *BMC Gastroenterol*. 2011; 11: 17.

201. **Dimidi E**, Christodoulides S, Fragkos KC, Scott SM, Whelan K. The effect of probiotics on functional constipation in adults: a systematic review and meta-analysis of randomized controlled trials. *Am J Clin Nutr*. 2014; 100(4): 1075-84.

202. **Severance EG**, Gressitt KL, Stallings CR, Katsafanas E, Schweinfurth LA, Savage CLG, Adamos MB, et. al. Probiotic normalization of Candida albicans in schizophrenia: A randomized, placebo-controlled, longitudinal pilot study. *Brain Behav Immun*. 2017; 62: 41-45.

203. **Tomasik J**, Yolken RH, Bahn S, Dickerson FB. Immunomodulatory Effects of Probiotic Supplementation in Schizophrenia Patients: A Randomized, Placebo-Controlled Trial. *Biomark Insights*. 2015; 10:47-54.

204**. Dickerson FB**, Stallings C, Origoni A, Katsafanas E, Savage CL, Schweinfurth LA, Goga J, Khushalani S, et. al. Effect of probiotic supplementation on schizophrenia symptoms and association with gastrointestinal functioning: a randomized, placebo-controlled trial. *Prim Care Companion CNS Disord*. 2014; 16(1): PCC.13m01579.

205. **Nagamine T**, Sato N, Seo G. Probiotics reduce negative symptoms of schizophrenia: A care report. International Medical Journal 2012; 19(No. 1): 67-68.

206**. Okubo R**, Koga M, Katsumata N, Odamaki T, Matsuyama S, Oka M, Narita H, et. al. Effect of bifidobacterium breve A-1 on anxiety and depressive symptoms in schizophrenia: A proof-of-concept study. *J Affect Disord.* 2019; 245: 377-385.

207. **Evans SJ**, Bassis CM, Hein R, Assari S, Flowers SA, Kelly MB, Young VB, et. al. The gut microbiome composition associates with bipolar disorder and illness severity. *J Psychiatr Res*. 2017; 87: 23-29.

208. **Coello K**, Hansen TH, Sørensen N, Munkholm K, Kessing LV, Pedersen O, Vinberg M. Gut microbiota composition in patients with newly diagnosed bipolar disorder and their unaffected first-degree relatives. *Brain Behav Immun*. 2019; 75: 112-118.

209. **Jiang H**, Ling Z, Zhang Y, Mao H, Ma Z, Yin Y, Wang W, et. al. Altered fecal microbiota composition in patients with major depressive disorder. *Brain Behav Immun*. 2015; 48: 186-94.

210. **Sokol H**, Seksik P, Furet JP, Firmesse O, Nion-Larmurier I, Beaugerie L, Cosnes J, et. al. Low counts of Faecalibacterium prausnitzii in colitis microbiota. *Inflamm Bowel Dis*. 2009; 15(8): 1183-9.

211. **Sherwin E**, Sandhu KV, Dinan TG, Cryan JF. May the Force Be With You: The Light and Dark Sides of the Microbiota-Gut-Brain Axis in Neuropsychiatry. *CNS Drugs*. 2016; 30(11): 1019-1041.

212. **Dickerson F**, Adamos M, Katsafanas E, Khushalani S, Origoni A, Savage C, Schweinfurth L, et. al. Adjunctive probiotic microorganisms to prevent rehospitalization in patients with acute mania: A randomized controlled trial. *Bipolar Disord*. 2018; 20(7): 614-621.

213. **Reininghaus EZ**, Wetzlmair LC, Fellendorf FT, Platzer M, Queissner R, Birner A, Pilz R, et. al. The Impact of Probiotic Supplements on Cognitive Parameters in Euthymic Individuals with Bipolar Disorder: A Pilot Study. *Neuropsychobiology*. 2018; 18: 1-8.

214. **Hutkins RW**, Krumbeck JA, Bindels LB, Cani PD, Fahey G Jr, Goh YJ, Hamaker B, et. al. Prebiotics: why definitions matter. *Curr Opin Biotechnol*. 2016; 37: 1-7.

215. **Nishida K**, Sawada D, Kuwano Y, Tanaka H, Sugawara T, Aoki Y, et al. Daily administration of paraprobiotic lactobacillus gasseri CP2305 ameliorates chronic stress-associated symptoms in japanese medical students. *Journal of functional foods* 2017; 36: 112-121.

216. **Wegh CAM**, Geerlings SY, Knol J, Roeselers G, Belzer C. Postbiotics and Their Potential Applications in Early Life Nutrition and Beyond. *Int J Mol Sci*. 2019; 20(19): 4673.

217. **Tessema A**. Lactic acid bacteria and culture media for the production of potential antivirulence peptides against salmonella typhimurium[dissertation]; 2015.

218. **Riaz Rajoka MS**, Zhao H, Mehwish HM, Li N, Lu Y, Lian Z, Shao D, et. al. Anti-tumor potential of cell free culture supernatant of Lactobacillus rhamnosus strains isolated from human breast milk. *Food Res Int*. 2019; 123: 286-297.

219. **Yasmin A**, Butt MS, Afzaal M, van Baak M, Nadeem MT, Shahid MZ. Prebiotics, gut microbiota and metabolic risks: Unveiling the relationship. *Journal of functional foods* 2015; 17: 189-201.

220. **Hill C**, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, Morelli L, et. al. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol*. 2014; 11(8): 506-14.

221. **Wilkinson MG**. Flow cytometry as a potential method of measuring bacterial viability in probiotic products: A review. *Trends in food science & technology* 2018; 78: 1-10.

222. **Patil S**, Sawant S, Hauff K, Hampp G. Validated Postbiotic Screening Confirms Presence of Physiologically-Active Metabolites, Such as Short-Chain Fatty Acids, Amino Acids and Vitamins in Hylak® Forte. *Probiotics Antimicrob Proteins*. 2019; 11(4): 1124-1131.

223. **Kalb SR**, Boyer AE, Barr JR. Mass Spectrometric Detection of Bacterial Protein Toxins and Their Enzymatic Activity. *Toxins (Basel)*. 2015; 7(9): 3497-511.

224. **Jeong JJ**, Kim KA, Ahn YT, Sim JH, Woo JY, Huh CS, Kim DH. Probiotic Mixture KF Attenuates Age-Dependent Memory Deficit and Lipidemia in Fischer 344 Rats. *J Microbiol Biotechnol*. 2015; 25(9): 1532-6.

225. **Liu J**, Sun J, Wang F, Yu X, Ling Z, Li H, Zhang H, et. al. Neuroprotective Effects of Clostridium butyricum against Vascular Dementia in Mice via Metabolic Butyrate. *Biomed Res Int*. 2015; 2015: 412946.

226. **Savignac HM**, Tramullas M, Kiely B, Dinan TG, Cryan JF. Bifidobacteria modulate cognitive processes in an anxious mouse strain. *Behav Brain Res*. 2015; 287: 59-72.

227. **Gareau MG**, Wine E, Rodrigues DM, Cho JH, Whary MT, Philpott DJ, Macqueen G, Sherman PM. Bacterial infection causes stress-induced memory dysfunction in mice. *Gut*. 2011; 60(3): 307-17.

228. **Davari S**, Talaei SA, Alaei H, Salami M. Probiotics treatment improves diabetes-induced impairment of synaptic activity and cognitive function: behavioral and electrophysiological proofs for microbiome-gut-brain axis. *Neuroscience*. 2013; 240: 287-96.

229. **Athari Nik Azm S**, Djazayeri A, Safa M, Azami K, Ahmadvand B, Sabbaghziarani F, Sharifzadeh M, et. al. Lactobacilli and bifidobacteria ameliorate memory and learning deficits and oxidative stress in β-amyloid (1-42) injected rats. *Appl Physiol Nutr Metab*. 2018; 43(7): 718-726.

230. **Wang QJ**, Shen YE, Wang X, Fu S, Zhang X, Zhang YN, Wang RT. Concomitant memantine and *Lactobacillus plantarum* treatment attenuates cognitive impairments in APP/PS1 mice. *Aging (Albany NY).* 2020; 12(1): 628-649.

231. **Liu YW**, Liu WH, Wu CC, Juan YC, Wu YC, Tsai HP, Wang S, et. al. Psychotropic effects of Lactobacillus plantarum PS128 in early life-stressed and naïve adult mice. *Brain Res*. 2016; 1631: 1-12.

232. **Liu WH**, Chuang HL, Huang YT, Wu CC, Chou GT, Wang S, Tsai YC. Alteration of behavior and monoamine levels attributable to Lactobacillus plantarum PS128 in germ-free mice. *Behav Brain Res*. 2016; 298(Pt B): 202-9.

233. **Smith CJ**, Emge JR, Berzins K, Lung L, Khamishon R, Shah P, Rodrigues DM, et. al. Probiotics normalize the gut-brain-microbiota axis in immunodeficient mice. *Am J Physiol Gastrointest Liver Physiol*. 2014; 307(8): G793-802.

234. **Luo J**, Wang T, Liang S, Hu X, Li W, Jin F. Ingestion of Lactobacillus strain reduces anxiety and improves cognitive function in the hyperammonemia rat. *Sci China Life Sci*. 2014; 57(3): 327-335.

235. **Savignac HM**, Kiely B, Dinan TG, Cryan JF. Bifidobacteria exert strain-specific effects on stress-related behavior and physiology in BALB/c mice. *Neurogastroenterol Motil*. 2014; 26(11): 1615-27.

236. **Ohland CL**, Kish L, Bell H, Thiesen A, Hotte N, Pankiv E, Madsen KL. Effects of Lactobacillus helveticus on murine behavior are dependent on diet and genotype and correlate with alterations in the gut microbiome. *Psychoneuroendocrinology*. 2013; 38(9): 1738-47.

237. **Bercik P**, Verdu EF, Foster JA, Macri J, Potter M, Huang X, Malinowski P, et. al. Chronic gastrointestinal inflammation induces anxiety-like behavior and alters central nervous system biochemistry in mice. *Gastroenterology*. 2010; 139(6): 2102-2112.e1.

238. **Bercik P**, Park AJ, Sinclair D, Khoshdel A, Lu J, Huang X, Deng Y, et. al. The anxiolytic effect of Bifidobacterium longum NCC3001 involves vagal pathways for gut-brain communication. *Neurogastroenterol Motil*. 2011; 23(12): 1132-9.

239. **Messaoudi M**, Lalonde R, Violle N, Javelot H, Desor D, Nejdi A, Bisson JF, et al. Assessment of psychotropic-like properties of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in rats and human subjects. *Br J Nutr.* 2011; 105(5): 755-64.

240. **Bravo JA**, Forsythe P, Chew MV, Escaravage E, Savignac HM, Dinan TG, Bienenstock J, et. al. Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. *Proc Natl Acad Sci U S A*. 2011; 108(38): 16050-5.

241. **Liang S**, Wang T, Hu X, Luo J, Li W, Wu X, Duan Y, et. al. Administration of Lactobacillus helveticus NS8 improves behavioral, cognitive, and biochemical aberrations caused by chronic restraint stress. *Neuroscience*. 2015; 310: 561-77.

242. **Desbonnet L**, Garrett L, Clarke G, Bienenstock J, Dinan TG. The probiotic Bifidobacteria infantis: An assessment of potential antidepressant properties in the rat. *J Psychiatr Res*. 2008; 43(2): 164-74.

243. **Desbonnet L**, Garrett L, Clarke G, Kiely B, Cryan JF, Dinan TG. Effects of the probiotic Bifidobacterium infantis in the maternal separation model of depression. *Neuroscience*. 2010; 170(4): 1179-88.

244. **Arseneault-Bréard J**, Rondeau I, Gilbert K, Girard SA, Tompkins TA, Godbout R, Rousseau G. Combination of Lactobacillus helveticus R0052 and Bifidobacterium longum R0175 reduces post-myocardial infarction depression symptoms and restores intestinal permeability in a rat model. *Br J Nutr*. 2012 Jun;107(12):1793-9.

245. **Eskelinen MH**, Ngandu T, Tuomilehto J, Soininen H, Kivipelto M. Midlife coffee and tea drinking and the risk of late-life dementia: a population-based CAIDE study. *J Alzheimers Dis*. 2009; 16(1): 85-91.

246. **Leblhuber F**, Steiner K, Schuetz B, Fuchs D, Gostner JM. Probiotic Supplementation in Patients with Alzheimer's Dementia - An Explorative Intervention Study. *Curr Alzheimer Res*. 2018; 15(12): 1106-1113.

247. **Agahi A**, Hamidi GA, Daneshvar R, Hamdieh M, Soheili M, Alinaghipour A, Esmaeili et. al. Does Severity of Alzheimer's Disease Contribute to Its Responsiveness to Modifying Gut Microbiota? A Double-Blind Clinical Trial. *Front Neurol.* 2018; 9: 662.

248**. Takada M**, Nishida K, Kataoka-Kato A, Gondo Y, Ishikawa H, Suda K, Kawai M, et. al. Probiotic Lactobacillus casei strain Shirota relieves stress-associated symptoms by modulating the gut-brain interaction in human and animal models. *Neurogastroenterol Motil*. 2016; 28(7): 1027-36.

249. **Rao AV**, Bested AC, Beaulne TM, Katzman MA, Iorio C, Berardi JM, Logan AC. A randomized, double-blind, placebo-controlled pilot study of a probiotic in emotional symptoms of chronic fatigue syndrome. *Gut Pathog*. 2009; 1(1): 6.

250. **Majeed** **M**, Nagabhushanam K, Arumugam S, Majeed S, Ali F. *Bacillus coagulans* MTCC 5856 for the management of major depression with irritable bowel syndrome: a randomised, double-blind, placebo controlled, multi-centre, pilot clinical study. *Food Nutr Res*. 2018; 62.

251. **Benton D**, Williams C, Brown A. Impact of consuming a milk drink containing a probiotic on mood and cognition. *Eur J Clin Nutr*. 2007; 61(3): 355-61.

252. **Steenbergen L**, Sellaro R, van Hemert S, Bosch JA, Colzato LS. A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood. *Brain Behav Immun*. 2015; 48: 258-64.

253. **Brenner LA**, Forster JE, Stearns-Yoder KA, Stamper CE, Hoisington AJ, Brostow DP, Mealer M, et. al. Evaluation of an Immunomodulatory Probiotic Intervention for Veterans With Co-occurring Mild Traumatic Brain Injury and Posttraumatic Stress Disorder: A Pilot Study. *Front Neurol.* 2020; 11: 1015.