**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* A1  Paraprobiotic: *B. breve* A1- heat killed  Postbiotic: 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 mice  Naive 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.

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