

Table 1 Clinical and preclinical evidence for the antidepressant and anxiolytic properties associated with targeting the gut microbiota (Adopted from Foster et al., 2017)

	Behavioural outcomes	Physiological outcomes
Clinical evidence		
B-GOS	Increased cognitive processing of positive versus negative attentional vigilance	Reduced cortisol awakening response
Lactobacillus casei strain Shirota	Reduced anxiety scores in patients with chronic fatigue syndrome Improved mood in individuals with a low mood prior to taking the probiotic	Increased numbers of Lactobacillus and Bifidobacterium in faecal samples NA
Probiotic formulation: Lactobacillus helveticus and Bifidobacterium longum	Reduced psychological distress as measured by the HADS	Reduced 24-h UFC levels
Multispecies probiotic formulation: Lactobacillus and Bifidobacterium species	Reduced cognitive processing of sad mood; decreased aggressive feelings and rumination	NA
Preclinical evidence		
Prebiotic- FOS and GOS	Antidepressant and anxiolytic-like effects in adult mice. Reversed the behavioural effects of chronic psychosocial stress in mice.	Increased BDNF, NR1 and NR2A mRNA, and protein expression in the dentate gyrus and frontal cortex. Reduced acute and chronic stress-induced corticosterone release. Modified specific gene expression in the hippocampus and hypothalamus. Reduced chronic stress-induced elevations in pro-inflammatory cytokines levels.
Prebiotic- 3'Sialyllactose and 6'sialyllactose	Anxiolytic effect in mice exposed to SDR	Prevented SDR-mediated reduction in the number of immature neurons
Prebiotic- GOS & polydextrose with lactoferrin (Lf) and milk fat globule membrane	Reduced immobility time of maternally separated rats in a forced swim test	Improves NREM Sleep, Enhance REM Sleep Rebound and Attenuate the Stress-Induced Decrease in Diurnal Temperature. Attenuated exaggerated IL-6 response in maternally separated rats following concanavalin A stimulation.
Bifidobacterium breve	Improved depressive and anxiety-related behaviours in mice	No effect upon circulating corticosterone
Bifidobacterium longum	Anxiolytic effect in step-down inhibitory avoidance	Anxiolytic effect mediated via the vagus nerve
Lactobacillus plantarum PS128	Reduced immobility time and increased sucrose preference in ELS mice	Decreased basal and stress-induced circulating corticosterone levels; attenuated circulating TNF- $\alpha$ and IL-6 levels while increasing IL-10 levels in ELS mice
Lactobacillus rhamnosus	Reduced immobility time in the forced swim test. Decreased stress-induced anxiety-like behaviour.	Decreased stress-induced circulating corticosterone secretion and altered central GABA receptor subunit expression. Attenuated chronic stress-related activation of dendritic cells while increasing IL-10 + regulatory T cells.
Lactobacillus fermentum NS9	Reduced ampicillin-induced anxiety behaviour	Decreased ampicillin-induced corticosterone secretion and increased hippocampal mineralocorticoid receptor and NMDA receptor levels.
Butyric acid	Reduced immobility time in Flinders sensitive line rats exposed to a forced swim test	Increased BDNF expression within the prefrontal cortex
	Behavioural outcomes	Physiological outcomes

Note: BDNF (brain-derived neurotrophic factor), ELS (early life stress-exposed), FOS (fructo-oligosaccharide), GABA ( $\gamma$ -aminobutyric acid), GOS (galacto-oligosaccharide), HADS (Hospital Anxiety and Depression Scale), IL (interleukin), mRNA (messenger RNA), NA (not assessed), NMDA (N-methyl-d-aspartate), SDR (social disruption stress), TNF (tumour necrosis factor), UFC (urinary free cortisol), NR (NMDA Receptor) (Adopted from Foster et al., 2017)