**TABLE S2 . Neuro-Psychological Disorders and the Gut Microbiome**

| **Neurological/ Psychological Disorder/Authora** | **Objectives/Purpose** | **Sample** | **Effect on Microbiome/Major findings** |
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| Depression (Kelly, J.R., Borre,Y.,O’Brien, D.,Patterson, E.,El Aidy,S., Deane, J....Dinan,T. (2016) | Human and rat study where fecal microbiota transplants from human participants, both depressed and controls, were transferred to microbiota-deficient rats. The purpose of the study was to confirm that a fecal microbiota transplant from depressed patients to a rat would change the behavior of the rat.  | Humann=34 major depressionn=33 matched healthy controlsFecal transplants-Pooled fecal samples were obtained from 3 of the most severely depressed male patients and 3 age and sex matched controlsRatsn=15 controln=13 depressed group Rats were given antibiotic cocktail 28 consecutive days prior to fecal transplant. Booster transplant were given twice a week during study.  | * Rats that received the fecal transplant from depressed patients displayed anxiety- like behavior and a significant decrease in sucrose intake. Other neurobiologic outcome measures were significantly different from control rats.
* Decreased gut microbiota richness and diversity was significantly different in rats that received the fecal transplant from depressed patients.
* Gut transit time in the rats that received the fecal transplant from depressed patients was significantly different.
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| Anxiety (Clarke et al., 2013)  | Animal study examining effect of microbiota on the CNS and effects on the serotonergic system \*; male/female differences and changes after colonizationA complex system located in the midbrain that is related to inhibition. Dysfunction has been linked to numerous to cognitive disorders (Berger, Gray, & Roth, 2009)  | GF and CC mice were randomly assigned to three groups:1) High performance liquid chromatography/PCR *n* = 9–10 2) Stress-induced cortisone production *n* = 9–103) Splenocyte stimulations*n* = 5–8Subsequent studyMale GF mice *n* = 9 were colonized produce the colonized GF. 3 groups (M/F mice); Germ free (GF); Conventionally Colonized (CC); & Colonized GF Adult mice were euthanized at 6–9 weeks. | * Blunted immune response in GF mice
* GF males exhibit less anxiety than CC or colonized GF animals
* As a result of absent gut microbiota CNS neurotransmission is significantly affected and has lifelong effects
	+ GF males have significant elevation in hippocampal concentration of 5-hydroxtryptamine and 5-hydroxyindoleacetic acid compared to CC animals
	+ Plasma tryptophan is increased in GF males which suggests a humoral route of microbiota influence on CNS serotonergic neurotransmission
	+ Other outcome measures: Brain derived neurotropic factor, serotonergic gene expression, 5-hydroxytryptamine (5-HT) tissue concentration in the hippocampus
* Absence of microflora in early life has significant hippocampal effects that are difficult to reverse later in life
* Colonization of GF mice does not exert effects on CNS; perhaps a consequence of absent microbiota despite normalization of tryptophan levels
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| Frailty, Health, & Depression(Claesson et al., 2012) | Examines the variation of human microbiota in the elderly and correlative effects on immune system and overall health | *n* = 191, 2 groups*n* = 178 > 64 years of age divided into 4 subgroups: 1) living in the community, 2) outpatient day hospital, 3) short-term rehab, 4) long-term institution; *n* = 13 young adult controls | * Diet that is diverse supports a healthy gut microbiome and a healthy gut microbiome is associated with good health
* Genera identified in the gut microbiome were specific to four living locations Markers of inflammation were higher in long stay and rehab members than in community dwellers
* Frailty/health deterioration were associated with loss of community microbiota or less diverse microbiome
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| Autism(Bresnahan et al., 2015) | Evaluates maternal report of infant and toddler gastrointestinal symptoms with risk for autism | Human study; Prospective maternal reported data from large national mother/child study in Norway. Children born 2002–2008; follow-up surveys at 18 and 36 months *n* = 45,126, Includes 3 groups:Typical Development (TD) *n* = 40,295; Autism Spectrum Disorder (ASD) *n* = 195; Delayed Development (DD) *n* = 4636 | * ASD children more likely to have maternally reported GI symptoms as infants and toddlers than children with TD or DD.
* ASD children were significantly different from TD children with increased odds for maternally reported
	+ constipation, food allergy/intolerance at 6–18 months of age
	+ 2-fold increase in having any GI symptom at 18–36 months of age
* ASD children were more likely to have maternally reported constipation as compared to DD and TD children
* 81% of children with ASD were male.
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| Autism/Social Development (Desbonnet, Clarke, Shanahan, Dinan, & Cryan, 2014) | Examination of the effects of germ free mice rearing conditions through early life on social behavior in adulthood | Male Mice, Germ Free (GF) mice; Conventionally Colonized (CC); | * Microbial diversity was reduced in the GF mice
* GF animals exhibited a decrease responsiveness 24 hours after first tested in the social transmission of food preference test compared to CC animals
* Microbiota are essential to developing social behaviors, motivations and regulators of repetitive behaviors
* BDNF in hippocampus decreased in GF mice. Brain–derived neurotropic factor essential for neuron support and growth .
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| Alzheimer’s disease(Bhattacharjee & Lukiw, 2013) | Reviews current evidence linking microbiome with Alzheimer’s disease | Review | * Relationships between the gut microbiome and neuro-immune system are not well understood
* Several studies have found relationships between nutrition and metabolic functioning and postulate effects to the immune system and metabolic disease
* Specific bacteria typically found in microbiome have been shown to assist by producing chemical compounds related to CNS formation, function and signaling. Decreases in certain neurotransmitters have also been found in patients with Alzheimer’s disease
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| Alzheimer’s disease(Naseer et al., 2014) | Discusses current evidence that explains the microbiome cascade effects on the development of obesity, Type II diabetes and Alzheimer’s disease | Review | * Obesity leads to development of Type II diabetes
* Type II diabetes is a risk factor for development of Alzheimer’s disease and similarly shares altered system functions (vascular and neurodegenerative effects)
* The gut microbiome exerts influence on the CNS, brain function and is theorized to exert effects via immune cells
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| Central Nervous & Immune System(Erny et al., 2015) | Evaluates the gut microbiome influence on CNS and immune system, specifically microglia | Mice (M/F); 2 groups; 1) Specific Pathogen Free (SPF) 2) Germ Free (GF)  | * An absent microbiome affects microglia growth and function
* Significant differences in microglia mRNA profiles of microglia genes were seen between groups (SPF & GF) which leads to altered responses
* Humoral signaling pathways appear to be the mechanism for gut-brain communication
* Proposes that continuous input from complex microbiota is required for microglia homeostasis throughout life
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| Pain, Stress, (O'Mahony et al., 2009) | Evaluating early life stress impact on the brain-gut axis, gut microbiota, behaviors, and immune, endocrine and visceral pain systems  | Rats *n* = 22; 2 groups*n* = 11 housed with mothers*n* = 11 maternally separated | * Separated mice had an altered gut microbiome as compared to controls
* Separated animals exhibited stress, anxiety and altered bowel habits, and increased visceral hypersensitivity (pain) compared to controls
* Study confirms link between stress and gut microbiota in separated animals
* Early life stress confers multiple immediate sustained effects to the brain-gut which could lead to stress-related disorders later in life
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| Cognitive Function (Davari, Talaei, Alaei, & Salami, 2013) | Examines the effect of probiotics on spatial learning and memory, hippocampal long term potentiation and oxidative stress in rats  | Rats (*n* = 40)4 groups, 10/group, 1) Control Group (CO); 2) Diabetic Controls (DC); 3) Controls with probiotic supplements (CP); 4) Diabetics with probiotic supplements (DP) | * CO animals had the best performance in spatial learning and memory DC had worst performance
* Treatment with probiotics significantly improved spatial learning and memory in all groups
* Diabetic animals were significantly inferior to control animals
	+ In spatial tasks, learning and memory tasks
	+ Had slowed conduction velocity in peripheral nervous systems
	+ Declined occurrence in long term potentiation in the CA1 area of hippocampus
* Probiotics reversed the behavioral and electrophysiological deficits in diabetic animals
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| Brain development, ageing and neurodegeneration (Dinan & Cryan, 2016) | Current review of the gut-brain axis and the role of the gut microbiota in this process. | Review | * Understanding the intricate gut –brain access is imperative
* Role of ageing on the gut microbiome
* Brain development and role of the microbiota
* Role of the gut microbiome as related to
	+ Depression
	+ Autism
	+ Schizophrenia
	+ Parkinson’s disease
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aReferences cited in text appear in the reference list; those cited only in this SDC are listed below.

Additional References

Dinan, T. G., & Cryan, J. F.(2016). Gut instincts: Microbiota as a key regulator of brain development, ageing and neurodegeneration. *Journal of Physiology.* Advance online publication.. doi: 10.1113/JP273106

Kelly, J. R., Borre, Y., O' Brien, C., Patterson, E., El Aidy, S., Deane, J., . . .Dinan, T. (2016) Transferring the blues: Depression-associated gut microbiota induces neurobehavioural changes in the rat. *Journal of Psychiatric Research*, 82:109-18. doi: 10.1016/j.jpsychires.2016.07.019