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The Gut – Brain Connection: How the Microbiome Influences Neuropsychiatric Disease

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Now the popular subject of dietary books and television programmes, the gut-brain connection in its vast complexityis becoming better understood. These critical organs communicate via bidirectional vagal nerve stimulation, gut-derived neurotransmitters like serotonin,andimmunological messengers controlled bygut microbiota [1-3]. This physiological communicationis reflected clinically in the high rates of gastrointestinal comorbidities observed in patients with neuropsychiatric illnesses like schizophrenia and autism [3,4]. The key to this connection may lie in the gut microbiome, which consists of over 1013 microorganisms living symbiotically in our gastrointestinal tract [5]. Neuropsychiatric medicationscommonly cause gastrointestinal symptoms and studies have shown that antidepressantsalter the microbiome [6], whilst antipsychotics can cause weight gain due to dysregulatedmicrobiota [7]. In turn, optimisation of the gut microbiome could improvesymptoms of neuropsychiatric illness, making it an excitingtherapeutic target.

Each individual's gut microbiome is unique, like a gastro-intestinal fingerprint. Microbiome profiles can therefore reveal clues pertaining todisease pathology. Genomic studies show that there is a significant difference in the microbiota profile of patients with depression compared to healthy controls,with reduced diversity andlower levels of Faecalibacterium [8]. A typical pattern of reduced lactobacillus species is seen in patients with schizophrenia [9], and significantly low levels of Prevotella in children with autism [10]. Patients with Parkinson's disease also have a distinct microbiome profile [11] and germ-free mice transplanted with faecal microbiota of Parkinson's disease patients develop motor deficits, unlike mice "humanized" with the microbiota of healthy controls [12]. This study illuminates an underlying causal link between an altered microbiome and neurological disease.

So what causes variations in microbiota that predispose their host to disease? The microbiome is shaped by its environment, as demonstrated by the different microbiotic profiles of people living in Malawi compared to the USA, in babies delivered vaginally or by C-section, and in adolescents growing up in urban versus rural environments [13-14]. This might help to explain the well-established but poorly understood effect of urbanicity as a risk factor for schizophrenia. The risk of schizophrenia with an urban upbringing is estimated to be 2.37 times higher than in a rural environment [15]. Greater immune activation after social stress testing has also been observed in subjects with an urban background [16]. Given the proposed immune origins of schizophrenia, based on elevated inflammatory markers in these patients [17], the microbiome may indeed explain this effect alongside other idiopathic symptoms of schizophrenia.

The study of germ-free mice, raised without exposure to microorganisms, provides particularly strong evidence for the role of the microbiota in neuropsychiatric disorders. For example, germ-free mice display decreased depressive-like behavior and better memory performance relative to controls [18]. Furthermore, beta amyloid plaques, the hallmark pathology of Alzheimer's disease, do not develop in germ-free mice, suggestingthe absence of a functioning microbiome may be protective against dementia [19]. Reduced sociability is observed in germ-free mice, which indicates that the gut microbiome is necessary for normal social behavior [20]. Interestingly, children with autism, whose social development is impaired, have a typically altered microbiome profile compared to healthy controls [21].

If microbiotadysbiosiscontributes toneuropsychiatric disease, restoration of the microbiome could theoretically alleviate symptoms. There is abundant evidence for the use of probiotics(supplements of beneficial bacteria) in neuropsychiatric illness. Probiotics reduce rates of rehospitalisation in bipolar disorder [22] and several clinical trials found them to have a positive impact on mood and cognition in depressed patients [23]. Faecal microbiotal transfer therapy is a novel technique for treating clostridium difficile diarrhoea, but has since been trialled for other conditions. For example, faecal transplant improvesboth behavioural and gastrointestinal symptoms in children with autism with positive effects persisting for at least 2 months [24]. Perhaps the most sustainable way of positively influencing the microbiome is by improvingour diet, as positedin the SMILES trial, which resulted in remission of depression in 32% of patients [25]. These studieshighlight the need for further classification of the microbiome,andencourage a fresh perspective of the human body as a holistic system dependent onhealthy interactions between all of its constituent parts.

References

1. Cryan JF, Dinan TG (2012) Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. Nat Rev Neurosci 13:701-712.
2. Forsythe P, Bienenstock J, Kunze WA (2014) Vagal pathways for microbiome-brain-gut axis communication. AdvExp Med Biol;817:115-133.
3. Severance EG, Prandovszky E, Castiglione J, Yolken RH (2015) Gastroenterology issues in schizophrenia: why the gut mat- ters. Curr Psychiatry Rep 17: 27.
4. Adams JB, Johansen LJ, Powell LD, Quig D, Rubin RA (2011) Gastrointestinal flora and gastrointestinal status in children with autism–comparisons to typical children and correlation with autism severity. BMC Gastroenterol 11: 22.
5. Gill SR, Pop M, DeBoy RT, Eckburg PB, Turnbaugh PJ, Samuel BS, et al. (2006) Metagenomic analysis of the human distal gut microbiome. Science 312: 1355-1359
6. Macedo D, Filho AJMC, Soares de Sousa CN, Quevedo J, Barichello T, Júnior HVN, Freitas de Lucena D (2017) Antidepressants, antimicrobials or both? Gut microbiotadysbiosis in depression and possible implications of the antimicrobial effects of antidepressant drugs for antidepressant effectiveness. J Affect Disord 208: 22-32.
7. Davey KJ, O'Mahony SM, Schellekens H, O'Sullivan O, Bienenstock J, Cotter PD, et al. (2012) Gender-dependent consequences of chronic olanzapine in the rat: effects on body weight, inflammatory, metabolic and microbiotaparamters. Psychopharmaclogy, 22: 155-169
8. Jiang H, Ling Z, Zhang Y, Mao H, Ma Z, Yin Y, Wang W, Tang W, Tan Z, Shi J, Li L, Ruan B (2015) Altered faecalmicrobiota composition in patients with major depressive disorder. Brain BehavImmunol Aug; 48: 186-94.
9. Schwarz E, Maukonen J, Hyytiäinen T, Kieseppä T, Orešič M, Sabunciyan S, Mantere O, Saarela M, Yolken R, Suvisaari J (2018) Analysis of microbiota in first episode psychosis identifies preliminary associations with symptom severity and treatment response. Schizophr Res 192: 398-403.
10. Kang DW, Park JG, Ilhan ZE, Wallstrom G, Labaer J, Adams JB, Krajmalnik-Brown R. (2013)Reduced incidence of prevotellaand other fermenters in intestinal microflora of autistic children. PLoS One 8: e68322.
11. Qian Y, Yang X, Xu S, Wu C, Song Y, Qin N, Chen SD, Xiao Q (2018) Alteration of the fecal microbiota in Chinese patients with Parkinson's disease. Brain BehavImmun 70: 194-202.
12. Sampson TR, Debelius JW, Thron T, Janssen S, Shastri GG, Ilhan ZE, Challis C, Schretter CE, Rocha S, Gradinaru V, Chesselet MF, Keshavarzian A, Shannon KM, Krajmalnik-Brown R, Wittung- Stafshede P, Knight R, Mazmanian SK (2016). Gut microbiota regulate motor deficits and neuroinflammation in a model of Parkinson's disease. Cell 167: 1469-1480
13. Yatsunenko T, Rey FE, Manary MJ, Trehan I, Dominguez-Bello MG, Contreras M, Magris M, Hidalgo G, Baldassano RN, Anokhin AP, Heath AC, Warner B, Reeder J, Kuczynski J, Caporaso JG, Lozupone CA, Lauber C, Clemente JC, Knights D, Knight R, Gordon JI (2012). Human gut microbiome viewed across age and geography. Nature. 486: 222-7.
14. M.G. Dominguez-Bello, E.K Costello, M. Contreras, M. Magris, G. Hidalgo, N. Fierer et al. (2010) Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. ProcNatlAcadSci :11971-11975.
15. Vassos E, Pederson CB, Murray RM, Collier DA, Lewis CM (2012)Meta-analysis of the association of urbanicity with schizophrenia. Schizophr Bull 38: 1118-1123.
16. Khandaker GM, Pearson RM, Zammit S, Lewis G, Jones PB (2014) Association of serum interleukin 6 and C-reactive protein in childhood with depression and psychosis in young adult life: A population-based longitudinal study. JAMA Psychiatry 71: 1121-1128.
17. Böbel TS, Hackl SB, Langgartner D, et al. (2018)Less immune activation following social stress in rural vs. urban participants raised with regular or no animal contact, respectively. Proceedings of the National Academy of Sciences of the United States of America;115: 5259-5264.
18. Zheng P, Zeng B, Zhou C, Liu M, Fang Z, Xu X, Zeng L, Chen J, Fan S, Du X, Zhang X, Yang D, Yang Y, Meng H, Li W, Melgiri ND,Licinio J, Wei H, Xie P (2016) Gut microbiome remodeling induces depressive-like behaviors through a pathway mediated by the host's metabolism. Mol Psychiatry 21: 786-796.
19. Harach T, Marungruang N, Duthilleul N, Cheatham V, Mc Coy KD, Frisoni G, Neher JJ, Fåk F, Jucker M, Lasser T, Bolmont T (2017) Reduction of abeta amyloid pathology in APPPS1 transgenic mice in the absence of gut microbiota. Sci Rep 7: 41802.
20. Luczynski P, McVey Neufeld KA, Oriach CS, Clarke G, Dinan TG, Cryan JF (2016). Growing up in a bubble: using germ-free ani- mals to assess the influence of the gut microbiota on brain and behavior. Int J Neuropsychopharmacol 19: 1-17.
21. Mulle JG, Sharp WG, Cubells JF (2013). The gut microbiome: a new frontier in autism research.Curr Psychiatry Rep 15: 337.
22. Dickerson F, Adamos M, Katsafanas E, Khushalani S, Origoni A, Savage C, Schweinfurth L, Stallings C, Sweeney K, Goga J, Yolken RH (2018) Adjunctive probiotic microorganisms to prevent rehospitalization in patients with acute mania: A randomised controlled trial. Bipolar Disord.
23. Wallace CJK, Milev R (2017) The effects of probiotics on depressive symptoms in humans: a systematic review. Ann Gen Psychiatry 16: 14.
24. Kang DW, Adams JB, Gregory AC, Borody T, Chittick L, Fasano A, Khoruts A, Geis E, Maldonado J, McDonough-Means S, Pollard EL, Roux S, Sadowsky MJ, Lipson KS, Sullivan MB, Caporaso JG, Krajmalnik-Brown R (2017) Microbiota transfer therapy alters gut ecosystem and improves gastrointestinal and autism symptoms: an open-label study. Microbiome 5: 10.
25. Jacka FN, O'Neil A, Opie R, Itsiopoulos C, Cotton S, Mohebbi M, Castle D, Dash S, Mihalopoulos C, Chatterton ML, Brazionis L, Dean OM, Hodge AM, Berk M (2017) A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial). BMC Med 15:23.