

The association of gut microbial composition with neurocognitive development in children: a systematic review and meta-analysis

E.J. Eyemienbai^{1,2}, E.M. O'Connor^{3–5} and A. Cremona^{2,4,6}

¹Health Service Executive (HSE), Limerick, Ireland,

²School of Allied Health, Faculty of Education and Health Sciences, University of Limerick, Limerick, Ireland,

³Department of Biological Sciences, Faculty of Science and Engineering, University of Limerick, Limerick, Ireland,

⁴Health Research Institute (HRI), University of Limerick, Limerick, Ireland,

⁵Alimentary Pharmabiotic Centre, Microbiome Ireland, University College Cork, Cork, Ireland and

⁶Irish Nutrition and Dietetics Institute (INDI), Dublin, Ireland

The association of the gut microbiota with neurological diseases and gastro-inflammatory diseases has been widely explored^(1,2), however, research on the association of gut microbial composition with neurocognitive development in children is lacking. The aim of this review is to synthesize data from existing literature to examine the relationship between gut microbial composition with neurodevelopmental parameters and the influence of covariates.

A systematic review was conducted according to CONSORT⁽³⁾ guidelines. Two independent researchers conducted the literature search with the following inclusion criteria: full text studies, published in English, children with no morbidity, cohort studied, and the exposure of interest was gut microbiota. Two independent reviewers extracted the data from the included studies and carried out a risk of bias quality assessment using Cochrane standards. A random effects model was used in reporting the effect of the meta-analysis. Heterogeneity of statistical results was assessed using the I².

Seven studies were synthesized in this review. Due to homogeneity only two studies were included in the meta-analysis. Temperament was the outcome of interest in three studies and cognitive development in four others. Results from the included studies showed that the influence of gut microbial composition on temperament domain scores was dependant on gender. *Bacteroides*, *Bifidobacterium*, *Eubacterium eligens*, *Roseburia hominis*, and *Adlercreutzia equolifaciens* were related to greater cognitive scoring while *Ruminococcus gnavus*, *Clostridiales* and *Faecalibacterium* were associated with poorer cognitive scoring. Findings from the meta-analysis on extraversion and negative affectivity showed low heterogeneity (95%CI = 2.15 [1.82, 2.47] I² = 46% p < 0.00001) with higher negative affectivity in both studies. Extraversion and orienting showed high heterogeneity (95%CI = -0.05 [-0.95, 0.86] I² = 98% p < 0.00001) with high extraversion in one study and high orienting in the other. Negative affectivity and orientating showed high heterogeneity (95%CI = -1.52 [-2.86, -0.18] I² = 99%) with higher negative affectivity in both studies. Extraversion, negative affectivity, and orienting are scales on The Early Childhood Behaviour Questionnaire⁽⁴⁾ (ECBQ) used in the assessment of temperament in children between 18 months to 36 months.

This systematic review collated evidence that gut microbial composition is associated with neurocognitive developmental parameters in children. The microbial clusters correlating with the mode of delivery at birth consisted of *V. dispar*, *Bacteroides* and *Bifidobacterium/Enterobacteriaceae*. *Bacteroides* predominance stereotypically occurred in infants born by vaginal delivery, while *V. dispar* was found in the highest percentage of children born by surgical delivery. The association between poor cognitive performance/ development and caesarean delivery may also be linked to reduced breastfeeding rates. Gut microbial abundance of *Bifidobacterium* and *Bacteroides* was associated with improved neurocognitive function and cognitive scores. Further research examining the mechanisms that influence the association between gut microbial composition and neurodevelopment in children is required.

References

1. Finegold SM, Summanen PH, Downes J, *et al.* (2017) *Anaerobe* **45**, 133–7.
2. Lin PW, Stoll BJ (2006) *The Lancet* **368**, 1271–83.
3. Schulz KF, Altman DG, Moher D (2010) *Ann Int Med* **152**.
4. Putnam SP, Gartstein MA, Rothbart MK (2006) *Infant Behav Dev* **29**, 386–401.