**Supplemental information**



Figure S1. Directed Acyclic Graph for determining confounders. Colors: black, predictors (G) and outcomes (B); gray, variables (Bm) and (RB) related to missingness; green, potential confounders that influence (G) and (B), including (A) and (DQ); orange, potential covariates of (G), including (DI), (CON), (AB), (DM), (SF), (BR), and (EX).



Figure S2. Beta diversity of the gut microbiota at the age of two, six, and 12 weeks. (a-e) Principal coordinate plots of beta diversity, based on different pairwise dissimilarity (Bray-Curtis and weighted Jaccard) and distance (UniFrac and Aitchison) matrices, with points and ellipses colored by ages (Lake blue, two weeks; Orange, six weeks; Purple, 12 weeks).



Figure S3. Beta diversity of the gut microbiota at the age of one and three years. (a-e) Principal coordinate plots of beta diversity, based on different pairwise dissimilarity (Bray-Curtis and weighted Jaccard) and distance (UniFrac and Aitchison) matrices, with points and ellipses colored by ages (Pink, one year; Grass green, three years).



Figure S4. Heatmap showing relative abundances of the gut microbiota at the genus level over time. Bacteria with average relative abundances lower than 1% across the first three years, were assigned to ‘Others’. Rows of bacteria were clustered based on Euclidean distance.

Table S1. Kendall correlations between behavioral measures.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | CBCL\_M\_Internalizing | | CBCL\_M\_Externalizing | | CBCL\_P\_Internalizing | | CBCL\_P\_Externalizing | | SDQ\_M\_Internalizing | | SDQ\_M\_Externalizing | | SDQ\_P\_Internalizing | | SDQ\_P\_Externalizing | | BRIEF-P\_M\_TotalScore | | BRIEF-P\_P\_TotalScore | | REEF\_M\_TotalScore | | REEF\_P\_TotalScore | | Flanker | | GiftWrap | | GiftDelay | | Whisper | |
| CBCL\_M\_Internalizing | | - | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  |
| CBCL\_M\_Externalizing | | 0.49\* | | - | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  |
| CBCL\_P\_Internalizing | | 0.4\* | | 0.21 | | - | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  |
| CBCL\_P\_Externalizing | | 0.32\* | | 0.29\* | | 0.54\* | | - | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  |
| SDQ\_M\_Internalizing | | 0.4\* | | 0.12 | | 0.21 | | 0.14 | | - | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  |
| SDQ\_M\_Externalizing | | 0.14 | | 0.39\* | | -0.02 | | 0.22 | | 0 | | - | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  |
| SDQ\_P\_Internalizing | | 0.3\* | | 0.17 | | 0.34\* | | 0.24 | | 0.31\* | | -0.06 | | - | |  | |  | |  | |  | |  | |  | |  | |  | |  |
| SDQ\_P\_Externalizing | | 0.11 | | 0.26 | | 0.16 | | 0.35\* | | 0.15 | | 0.32\* | | 0.18 | | - | |  | |  | |  | |  | |  | |  | |  | |  |
| BRIEF-P\_M\_TotalScore | | 0.44\* | | 0.53\* | | 0.27 | | 0.24 | | 0.2 | | 0.29\* | | 0.18 | | 0.22 | | - | |  | |  | |  | |  | |  | |  | |  |
| BRIEF-P\_P\_TotalScore | | 0.32\* | | 0.21 | | 0.38\* | | 0.37\* | | 0.27 | | 0.21 | | 0.38\* | | 0.23 | | 0.39\* | | - | |  | |  | |  | |  | |  | |  |
| REEF\_M\_TotalScore | | -0.19 | | -0.27\* | | -0.21 | | -0.18 | | -0.1 | | -0.16 | | -0.09 | | 0.03 | | -0.34\* | | -0.21 | | - | |  | |  | |  | |  | |  |
| REEF\_P\_TotalScore | | 0.02 | | -0.19 | | -0.03 | | -0.23 | | -0.01 | | -0.34\* | | -0.09 | | -0.25 | | -0.13 | | -0.13 | | 0.24 | | - | |  | |  | |  | |  |
| Flanker | | -0.01 | | 0.02 | | -0.18 | | -0.02 | | 0.08 | | 0.01 | | 0.04 | | 0.09 | | 0.01 | | -0.16 | | 0.07 | | 0.04 | | - | |  | |  | |  |
| GiftWrap | | -0.07 | | -0.03 | | 0.06 | | 0.05 | | 0 | | -0.09 | | -0.09 | | 0.17 | | 0.02 | | 0.01 | | 0.15 | | 0.1 | | 0.05 | | - | |  | |  |
| GiftDelay | | 0.06 | | 0.02 | | 0.15 | | 0.29\* | | 0.14 | | -0.17 | | 0.22 | | 0.2 | | 0.01 | | 0 | | 0.18 | | 0.07 | | 0.19 | | 0.11 | | - | |  |
| Whisper | | -0.06 | | -0.04 | | -0.1 | | -0.09 | | -0.01 | | -0.1 | | -0.21 | | -0.21 | | -0.14 | | -0.23 | | 0.21 | | 0.19 | | 0.11 | | -0.04 | | 0.25\* | | - |
| M, Mother; P, Partner; CBCL, the Child Behavioral Checklist; SDQ, the Strengths and Difficulties Questionnaire; BRIEF-P, Behavior Rating Inventory of Executive Functions - Preschool; REEF, Ratings of Everyday Executive Functioning. Note that increased internalizing and externalizing scores refer to more corresponding behavioral problems. A higher score on the BRIEF-P indicates worse executive functions while a higher score on the REEF indicates better executive functions. Higher scores on the four behavioral tasks mean better performances in inhibitory control. \* indicates a p value lower than 0.05. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

Table S2. Reliability of parental questionnaires.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Filler | Questionnaire | behavior | ωtotal | Cronbach's α |
| Mother | CBCL | Internalizing | IC | 0.83 |
| Externalizing | 0.92 | - |
| SDQ | Internalizing | 0.65 | - |
| Externalizing | 0.74 | - |
| BRIEF-P | Executive functions | 0.94 | - |
| REEF | Executive functions | IC | 0.96 |
| Partner | CBCL | Internalizing | IC | 0.83 |
| Externalizing | 0.84 | - |
| SDQ | Internalizing | 0.65 | - |
| Externalizing | 0.72 | - |
| BRIEF-P | Executive functions | IC | 0.95 |
| REEF | Executive functions | IC | 0.95 |
| IC indicates the estimate was incalculable. Due to better ability at assessing reliability, ωtotal values were used as the first important estimates in determining reliability. For those subscales and questionnaires with incalculable ωtotal, Cronbach's α values were computed as alternatives. All estimates were above 0.65, of which most of estimates were higher than 0.7, indicating good reliability of the scales. | | | | |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Proportion of missing values | | | | |
|  | 2w | 6w | 12w | 1y | 3y |
| CBCL\_M\_Internalizing | 16.7% | 14.3% | 13.7% | 12.5% | 3.1% |
| CBCL\_M\_Externalizing | 16.7% | 14.3% | 13.7% | 12.5% | 3.1% |
| SDQ\_M\_Internalizing | 16.7% | 14.3% | 13.7% | 12.5% | 3.1% |
| SDQ\_M\_Externalizing | 16.7% | 14.3% | 13.7% | 12.5% | 3.1% |
| BRIEF-P\_M\_TotalScore | 15.2% | 12.9% | 12.3% | 11.1% | 1.6% |
| REEF\_M\_TotalScore | 16.7% | 14.3% | 13.7% | 12.5% | 3.1% |
| Flanker | 40.9% | 35.7% | 37% | 34.7% | 26.6% |
| Whisper | 19.7% | 17.1% | 17.8% | 15.3% | 6.2% |
| Gift Wrap | 21.2% | 20% | 19.2% | 16.7% | 6.2% |
| Gift Delay | 19.7% | 18.6% | 17.8% | 15.3% | 4.7% |
| Notes. M, Mother; CBCL, the Child Behavioral Checklist; SDQ, the Strengths and Difficulties Questionnaire; BRIEF-P, Behavior Rating Inventory of Executive Functions - Preschool; REEF, Ratings of Everyday Executive Functioning. | | | | | |

Table S3. Proportion of missing values in problem behavior and executive functions.

Table S4. Differentially abundant microbial taxa at the genus level over time with linear discriminant analysis (LDA) scores higher than 2.

|  |  |  |
| --- | --- | --- |
| **Enriched age** | **Genus** | **LDA score** |
| 2 w | *Enterobacteriaceae* unidentified genus | 4.93 |
| 2 w | *Streptococcus* | 4.56 |
| 2 w | *Staphylococcus* | 4.43 |
| 2 w | [*Ruminococcus*] *gnavus* group | 4.3 |
| 2 w | *Enterococcus* | 4.1 |
| 2 w | *Clostridium* sensu stricto 1 | 3.99 |
| 2 w | *Parabacteroides* | 3.84 |
| 2 w | *Finegoldia* | 2.49 |
| 2 w | *Negativicoccus* | 2.3 |
| 6 w | *Lactobacillus* | 4.31 |
| 6 w | *Actinomyces* | 3.99 |
| 6 w | *Hungatella* | 3.42 |
| 6 w | *Megasphaera* | 3.4 |
| 6 w | *Candidatus* *Stoquefichus* | 2.5 |
| 6 w | *Halomonas* | 2.49 |
| 6 w | *Aeribacillus* | 2.12 |
| 12 w | *Bifidobacterium* | 5.3 |
| 12 w | *Bacteroides* | 4.54 |
| 12 w | *Rothia* | 2.85 |
| 12 w | *Varibaculum* | 2.85 |
| 12 w | *Ruminiclostridium* | 2.15 |
| 1 y | *Faecalibacterium* | 4.69 |
| 1 y | *Anaerostipes* | 4.32 |
| 1 y | *Veillonella* | 4.23 |
| 1 y | *Akkermansia* | 4.01 |
| 1 y | *Lachnoclostridium* | 3.79 |
| 1 y | *Erysipelatoclostridium* | 3.77 |
| 1 y | *Lachnospira* | 3.75 |
| 1 y | [*Eubacterium*] *eligens* group | 3.55 |
| 1 y | *Prevotella* 2 | 3.38 |
| 1 y | [*Clostridium*] *innocuum* group | 3.38 |
| 1 y | *Flavonifractor* | 3.2 |
| 1 y | *Sutterella* | 3.16 |
| 1 y | *Tyzzerella* 4 | 3.09 |
| 1 y | *Lachnospiraceae* UCG-004 | 3.08 |
| 1 y | *Eggerthella* | 2.98 |
| 1 y | *Parasutterella* | 2.97 |
| 1 y | *Clostridioides* | 2.67 |
| 1 y | *Tyzzerella* 3 | 2.6 |
| 1 y | CAG:352 | 2.54 |
| 1 y | *Lactococcus* | 2.48 |
| 3 y | *Blautia* | 4.78 |
| 3 y | *Prevotella* 9 | 4.56 |
| 3 y | *Ruminococcus* 2 | 4.31 |
| 3 y | *Fusicatenibacter* | 4.09 |
| 3 y | *Roseburia* | 4.08 |
| 3 y | *Subdoligranulum* | 4.06 |
| 3 y | *Dialister* | 4.03 |
| 3 y | [*Eubacterium*] *hallii* group | 3.88 |
| 3 y | *Erysipelotrichaceae* UCG-003 | 3.87 |
| 3 y | *Dorea* | 3.85 |
| 3 y | *Lachnospiraceae* ND3007 group | 3.79 |
| 3 y | *Ruminococcus* 1 | 3.74 |
| 3 y | *Lachnospiraceae* NK4A136 group | 3.65 |
| 3 y | *Intestinibacter* | 3.65 |
| 3 y | [*Eubacterium*] *coprostanoligenes* group | 3.65 |
| 3 y | [*Ruminococcus*] *torques* group | 3.58 |
| 3 y | *Ruminococcaceae* UCG-002 | 3.53 |
| 3 y | *Alistipes* | 3.5 |
| 3 y | uncultured genus | 3.49 |
| 3 y | *Christensenellaceae* R-7 group | 3.45 |
| 3 y | *Romboutsia* | 3.42 |
| 3 y | *Phascolarctobacterium* | 3.41 |
| 3 y | *Butyricicoccus* | 3.4 |
| 3 y | *Coprococcus* 2 | 3.4 |
| 3 y | uncultured bacterium | 3.35 |
| 3 y | [*Ruminococcus*] *gauvreauii* group | 3.33 |
| 3 y | *Barnesiella* | 3.26 |
| 3 y | *Coprococcus* 3 | 3.25 |
| 3 y | *Prevotella* 7 | 3.2 |
| 3 y | *Senegalimassilia* | 3.14 |
| 3 y | *Coprococcus* 1 | 3.06 |
| 3 y | *Ruminococcaceae* UCG-013 | 3.02 |
| 3 y | *Holdemanella* | 2.99 |
| 3 y | *Paraprevotella* | 2.99 |
| 3 y | *Terrisporobacter* | 2.98 |
| 3 y | [*Eubacterium*] *ventriosum* group | 2.98 |
| 3 y | *Ruminococcaceae* NK4A214 group | 2.94 |
| 3 y | *Sarcina* | 2.93 |
| 3 y | *Ruminococcaceae* UCG-005 | 2.93 |
| 3 y | *Sellimonas* | 2.9 |
| 3 y | [*Eubacterium*] *ruminantium* group | 2.81 |
| 3 y | *Lachnospiraceae* UCG-001 | 2.81 |
| 3 y | *Ruminiclostridium* 6 | 2.8 |
| 3 y | *Lachnospiraceae* FCS020 group | 2.78 |
| 3 y | *Ruminococcaceae* UCG-014 | 2.76 |
| 3 y | *Ruminococcaceae* UCG-004 | 2.75 |
| 3 y | *Adlercreutzia* | 2.67 |
| 3 y | *Lachnospiraceae* UCG-003 | 2.64 |
| 3 y | CAG:56 | 2.63 |
| 3 y | [*Eubacterium*] *xylanophilum* group | 2.63 |
| 3 y | *Alloprevotella* | 2.62 |
| 3 y | *Gordonibacter* | 2.54 |
| 3 y | *Ruminiclostridium* 5 | 2.53 |
| 3 y | *Ruminococcaceae* UCG-003 | 2.52 |
| 3 y | *Turicibacter* | 2.51 |
| 3 y | *Butyrivibrio* | 2.5 |
| 3 y | Family XIII AD3011 group | 2.45 |
| 3 y | *Odoribacter* | 2.4 |
| 3 y | *Mollicutes* RF39 uncultured bacterium | 2.4 |
| 3 y | *Oscillibacter* | 2.36 |
| 3 y | *Anaeroplasma* | 2.23 |
| 3 y | *Methanobrevibacter* | 2.22 |
| 3 y | *Marvinbryantia* | 2.15 |
| 3 y | *Butyricimonas* | 2.1 |
| 3 y | *Ruminiclostridium* 9 | 2.09 |

Table S5. Pearson correlations between actual and predicted results from random forest models.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Behavior at age three | Age of the gut microbiota | Median of Pearson correlation coefficient | Permutation *p* value | Adjusted permutation *p* value |
| CBCL\_M\_Internalizing | 2w | 0.04 | 0.91 | 1.00 |
| 6w | 0.05 | 0.87 | 1.00 |
| 12w | 0.02 | 0.96 | 1.00 |
| 1y | -0.09 | 0.80 | 1.00 |
| 3y | -0.16 | 0.59 | 1.00 |
| CBCL\_M\_Externalizing | 2w | 0.00 | 0.99 | 1.00 |
| 6w | -0.33 | 0.32 | 1.00 |
| 12w | 0.13 | 0.71 | 1.00 |
| 1y | 0.09 | 0.78 | 1.00 |
| 3y | -0.11 | 0.73 | 1.00 |
| SDQ\_M\_Internalizing | 2w | 0.05 | 0.88 | 1.00 |
| 6w | -0.03 | 0.91 | 1.00 |
| 12w | 0.28 | 0.37 | 1.00 |
| 1y | -0.16 | 0.67 | 1.00 |
| 3y | 0.06 | 0.85 | 1.00 |
| SDQ\_M\_Externalizing | 2w | 0.05 | 0.88 | 1.00 |
| 6w | -0.29 | 0.37 | 1.00 |
| 12w | 0.10 | 0.78 | 1.00 |
| 1y | 0.02 | 0.94 | 1.00 |
| 3y | 0.14 | 0.67 | 1.00 |
| BRIEF-P\_M\_TotalScore | 2w | 0.12 | 0.70 | 1.00 |
| 6w | 0.07 | 0.85 | 1.00 |
| 12w | 0.10 | 0.77 | 1.00 |
| 1y | 0.06 | 0.82 | 1.00 |
| 3y | -0.09 | 0.76 | 1.00 |
| REEF\_M\_TotalScore | 2w | -0.15 | 0.65 | 1.00 |
| 6w | -0.07 | 0.84 | 1.00 |
| 12w | -0.15 | 0.66 | 1.00 |
| 1y | -0.01 | 0.99 | 1.00 |
| 3y | -0.11 | 0.74 | 1.00 |
| Flanker | 2w | -0.07 | 0.83 | 1.00 |
| 6w | 0.32 | 0.32 | 1.00 |
| 12w | 0.07 | 0.84 | 1.00 |
| 1y | -0.17 | 0.63 | 1.00 |
| 3y | 0.07 | 0.83 | 1.00 |
| Whisper | 2w | 0.09 | 0.82 | 1.00 |
| 6w | -0.06 | 0.88 | 1.00 |
| 12w | 0.23 | 0.52 | 1.00 |
| 1y | 0.28 | 0.37 | 1.00 |
| 3y | -0.03 | 0.93 | 1.00 |
| GiftWrap | 2w | 0.02 | 0.94 | 1.00 |
| 6w | 0.25 | 0.39 | 1.00 |
| 12w | 0.14 | 0.67 | 1.00 |
| 1y | -0.02 | 0.93 | 1.00 |
| 3y | -0.37 | 0.23 | 1.00 |
| GiftDelay | 2w | -0.15 | 0.56 | 1.00 |
| 6w | -0.09 | 0.89 | 1.00 |
| 12w | 0.00 | 1.00 | 1.00 |
| 1y | 0.32 | 0.32 | 1.00 |
| 3y | 0.04 | 0.91 | 1.00 |
| N=1000 permutation tests were performed. | |  |  |  |
| FDR adjustments were conducted to the p values. | | |  |  |

Table S6. Microbial taxa and alpha diversity with confident age-stratified relations to behavioral measures and taxa prevalence over time.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Type** | **Behavior at age three** | **Taxa or alpha diversity** | **Prevalence**  **at 2w** | **Prevalence**  **at 6w** | **Prevalence**  **at 12w** | **Prevalence**  **at 1y** | **Prevalence**  **at 3y** | **Prevalence >10% at all ages** | **Prevalence > 10% only at the first three ages** | **Prevalence > 10% only at the last two ages** |
| genus | CBCL\_Internalizing | *Barnesiella* | 0 | 1 | 0 | 7 | 50 | no | no | no |
| genus | CBCL\_Internalizing | *Intestinibacter* | 0 | 9 | 16 | 78 | 88 | no | no | no |
| genus | CBCL\_Externalizing | *Barnesiella* | 0 | 1 | 0 | 7 | 50 | no | no | no |
| genus | CBCL\_Externalizing | *Butyricicoccus* | 0 | 0 | 3 | 56 | 89 | no | no | yes |
| genus | CBCL\_Externalizing | *Clostridium* sensu stricto 1 | 33 | 50 | 44 | 62 | 83 | yes | no | no |
| genus | CBCL\_Externalizing | *Parabacteroides* | 35 | 34 | 36 | 44 | 83 | yes | no | no |
| genus | CBCL\_Externalizing | *Streptococcus* | 94 | 93 | 88 | 90 | 88 | yes | no | no |
| genus | SDQ\_Internalizing | [*Ruminococcus*] *torques* group | 5 | 6 | 4 | 32 | 84 | no | no | yes |
| genus | SDQ\_Internalizing | *Bifidobacterium* | 79 | 87 | 93 | 99 | 100 | yes | no | no |
| genus | SDQ\_Internalizing | *Blautia* | 6 | 11 | 14 | 90 | 100 | no | no | no |
| genus | SDQ\_Internalizing | *Ruminococcus* 2 | 0 | 0 | 0 | 39 | 94 | no | no | yes |
| genus | SDQ\_Internalizing | *Sutterella* | 8 | 10 | 12 | 46 | 61 | no | no | no |
| genus | SDQ\_Externalizing | *Bifidobacterium* | 79 | 87 | 93 | 99 | 100 | yes | no | no |
| genus | SDQ\_Externalizing | *Butyricicoccus* | 0 | 0 | 3 | 56 | 89 | no | no | yes |
| genus | SDQ\_Externalizing | *Enterobacteriaceae* unidentified genus | 89 | 93 | 97 | 68 | 31 | yes | no | no |
| genus | SDQ\_Externalizing | *Halomonas* | 12 | 11 | 12 | 0 | 0 | no | yes | no |
| genus | SDQ\_Externalizing | *Oscillibacter* | 0 | 0 | 0 | 4 | 22 | no | no | no |
| genus | SDQ\_Externalizing | *Parabacteroides* | 35 | 34 | 36 | 44 | 83 | yes | no | no |
| genus | BRIEF-P | *Blautia* | 6 | 11 | 14 | 90 | 100 | no | no | no |
| genus | BRIEF-P | *Clostridium* sensu stricto 1 | 33 | 50 | 44 | 62 | 83 | yes | no | no |
| genus | BRIEF-P | *Halomonas* | 12 | 11 | 12 | 0 | 0 | no | yes | no |
| genus | BRIEF-P | *Intestinibacter* | 0 | 9 | 16 | 78 | 88 | no | no | no |
| genus | BRIEF-P | *Ruminococcus* 2 | 0 | 0 | 0 | 39 | 94 | no | no | yes |
| genus | BRIEF-P | *Streptococcus* | 94 | 93 | 88 | 90 | 88 | yes | no | no |
| genus | REEF | [*Ruminococcus*] *torques* group | 5 | 6 | 4 | 32 | 84 | no | no | yes |
| genus | REEF | *Halomonas* | 12 | 11 | 12 | 0 | 0 | no | yes | no |
| genus | REEF | *Lachnospiraceae* unidentified genus | 5 | 4 | 15 | 78 | 100 | no | no | no |
| genus | REEF | *Parabacteroides* | 35 | 34 | 36 | 44 | 83 | yes | no | no |
| genus | Flanker | *Anaerostipes* | 0 | 1 | 3 | 96 | 100 | no | no | yes |
| genus | Flanker | *Bacteroides* | 56 | 59 | 66 | 86 | 97 | yes | no | no |
| genus | Flanker | *Ruminococcaceae* UCG-013 | 0 | 0 | 0 | 33 | 73 | no | no | yes |
| genus | Flanker | *Subdoligranulum* | 2 | 0 | 0 | 31 | 95 | no | no | yes |
| genus | Flanker | *Sutterella* | 8 | 10 | 12 | 46 | 61 | no | no | no |
| genus | GiftWrap | *Coprococcus* 3 | 0 | 0 | 0 | 14 | 66 | no | no | yes |
| genus | GiftWrap | *Lachnospiraceae* NK4A136 group | 0 | 0 | 0 | 38 | 89 | no | no | yes |
| genus | GiftWrap | *Subdoligranulum* | 2 | 0 | 0 | 31 | 95 | no | no | yes |
| genus | GiftWrap | *Veillonella* | 62 | 64 | 62 | 71 | 17 | yes | no | no |
| alpha diversity | CBCL\_Internalizing | chao1 | - | - | - | - | - | - | - | - |
| alpha diversity | REEF | chao1 | - | - | - | - | - | - | - | - |
| alpha diversity | GiftWrap | chao1 | - | - | - | - | - | - | - | - |
| alpha diversity | GiftWrap | PD | - | - | - | - | - | - | - | - |

Table S7. The multilevel Bayesian results of selected genera and alpha diversity with behavioral measures.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Behavior at age three** | **Taxa or alpha diversity** | **Age of the gut microbiota** | **Rhat<1.01** | **Estimate** | **Estimate error** | **95% CI** | **95% CI excluding 0** |
| CBCL\_Externalizing | *Clostridium* sensu stricto 1 | 2w, 6w, 12w, 1y, 3y | yes | 0 | 0 | [-0.01, 0.01] | no |
| CBCL\_Externalizing | *Parabacteroides* | 2w, 6w, 12w, 1y, 3y | no | - | - | - | - |
| CBCL\_Externalizing | *Streptococcus* | 2w, 6w, 12w, 1y, 3y | yes | 0.03 | 0.02 | [0, 0.07] | no |
| SDQ\_Internalizing | *Bifidobacterium* | 2w, 6w, 12w, 1y, 3y | yes | 0.09 | 0.07 | [-0.04, 0.22] | no |
| SDQ\_Externalizing | *Bifidobacterium* | 2w, 6w, 12w, 1y, 3y | yes | -0.04 | 0.07 | [-0.17, 0.09] | no |
| SDQ\_Externalizing | *Enterobacteriaceae* unidentified genus | 2w, 6w, 12w, 1y, 3y | yes | 0.01 | 0.01 | [-0.01, 0.03] | no |
| SDQ\_Externalizing | *Parabacteroides* | 2w, 6w, 12w, 1y, 3y | no | - | - | - | - |
| BRIEF-P | *Clostridium* sensu stricto 1 | 2w, 6w, 12w, 1y, 3y | yes | 0 | 0 | [0, 0.01] | no |
| BRIEF-P | *Streptococcus* | 2w, 6w, 12w, 1y, 3y | yes | 0.05 | 0.02 | [0.02, 0.09] | yes |
| REEF | *Parabacteroides* | 2w, 6w, 12w, 1y, 3y | no | - | - | - | - |
| Flanker | *Bacteroides* | 2w, 6w, 12w, 1y, 3y | no | - | - | - | - |
| GiftWrap | *Veillonella* | 2w, 6w, 12w, 1y, 3y | yes | 0.01 | 0 | [0, 0.02] | no |
| CBCL\_Internalizing | chao1 | 2w, 6w, 12w, 1y, 3y | yes | -0.01 | 0.02 | [-0.06, 0.04] | no |
| REEF | chao1 | 2w, 6w, 12w, 1y, 3y | yes | 0.04 | 0.03 | [-0.01, 0.09] | no |
| GiftWrap | chao1 | 2w, 6w, 12w, 1y, 3y | yes | 0.02 | 0.03 | [-0.03, 0.07] | no |
| GiftWrap | PD | 2w, 6w, 12w, 1y, 3y | yes | 0.05 | 0.03 | [-0.01, 0.12] | no |
| CBCL\_Externalizing | *Parabacteroides* | 2w, 6w, 12w | no | - | - | - | - |
| SDQ\_Externalizing | *Halomonas* | 2w, 6w, 12w | no | - | - | - | - |
| SDQ\_Externalizing | *Parabacteroides* | 2w, 6w, 12w | no | - | - | - | - |
| BRIEF-P | *Halomonas* | 2w, 6w, 12w | no | - | - | - | - |
| REEF | *Halomonas* | 2w, 6w, 12w | no | - | - | - | - |
| REEF | *Parabacteroides* | 2w, 6w, 12w | no | - | - | - | - |
| Flanker | *Bacteroides* | 2w, 6w, 12w | yes | 0.01 | 0.01 | [-0.01, 0.03] | no |
| CBCL\_Externalizing | *Butyricicoccus* | 1y, 3y | yes | -0.01 | 0.08 | [-0.17, 0.15] | no |
| CBCL\_Externalizing | *Parabacteroides* | 1y, 3y | no | - | - | - | - |
| SDQ\_Internalizing | [*Ruminococcus*] *torques* group | 1y, 3y | yes | -0.22 | 0.07 | [-0.35, -0.07] | yes |
| SDQ\_Internalizing | *Ruminococcus* 2 | 1y, 3y | yes | -0.1 | 0.08 | [-0.26, 0.05] | no |
| SDQ\_Externalizing | *Butyricicoccus* | 1y, 3y | yes | -0.09 | 0.09 | [-0.25, 0.08] | no |
| SDQ\_Externalizing | *Parabacteroides* | 1y, 3y | yes | -0.04 | 0.03 | [-0.09, 0.02] | no |
| BRIEF-P | *Ruminococcus* 2 | 1y, 3y | yes | -0.11 | 0.08 | [-0.25, 0.04] | no |
| REEF | [*Ruminococcus*] *torques* group | 1y, 3y | yes | -0.05 | 0.08 | [-0.21, 0.09] | no |
| REEF | *Parabacteroides* | 1y, 3y | yes | -0.01 | 0.03 | [-0.06, 0.05] | no |
| Flanker | *Anaerostipes* | 1y, 3y | yes | -0.05 | 0.09 | [-0.23, 0.11] | no |
| Flanker | *Bacteroides* | 1y, 3y | yes | -0.07 | 0.08 | [-0.23, 0.08] | no |
| Flanker | *Ruminococcaceae* UCG-013 | 1y, 3y | yes | 0.1 | 0.1 | [-0.09, 0.29] | no |
| Flanker | *Subdoligranulum* | 1y, 3y | no | - | - | - | - |
| GiftWrap | *Coprococcus* 3 | 1y, 3y | no | - | - | - | - |
| GiftWrap | *Lachnospiraceae* NK4A136 group | 1y, 3y | yes | -0.07 | 0.05 | [-0.17, 0.01] | no |
| GiftWrap | *Subdoligranulum* | 1y, 3y | yes | -0.03 | 0.06 | [-0.16, 0.06] | no |
| Notes. Multilevel Bayesian linear regression models were performed on taxa and alpha diversity over time. Relations in gray rows are confident with 95% CI excluding zero. Chains were regarded converged when Rhat values lower than 1.01. Models that did not meet the Rhat criteria under current settings were not considered in the present study. Given that *Parabacteroides* and *Bacteroides* did not meet the Rhat requirement in the pooled data of all five ages, we did extra trajectory analyses for them after splitting the data into two periods (2w, 6w, and 12w; 1y and 3y; colored in gray). | | | | | | | |

Table S8. Overview of the associations in our study in comparison with findings reported in literature.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Microbial taxa and alpha diversity** | **In the present study** | **Literature about problem behavior or executive functions and inhibitory control** | **Other literature with similar findings** | **Other literature with divergent findings** | **Potential mechanisms** |
| ↑*Parabacteroides* (2w) | ↓ Externalizing behavior | NF | ↓ Parabacteroides in children with ASD  (Strati et al., 2017; Averina et al., 2020) | ↑*Parabacteroides* in Children with ASD (Inoue et al., 2016) | GABA |
|  | ↑ Executive functions | NF | ↓*Parabacteroides* in ADHD (Prehn-Kristensen et al., 2018) |  |  |
| ↑*Parabacteroides* (1y) | ↓ Externalizing behavior | NF |  |  |  |
| ↑*Ruminococcus* 2 (1y) | ↓ Internalizing behavior | NF | ↓*Ruminococcus* 2 in MDD patients (Cheung et al., 2019; Haiyin Jiang et al., 2015) |  | Tryptophan/ serotonin |
|  | ↑ Executive functions | NF |  | ↑ *Ruminococcaceae* in ADHD patients,and inattention (Szopinska-Tokov et al., 2020) |  |
| ↑ [*Ruminococcus*] *Torques* group (3y) | ↓ Executive functions | NF |  |  |  |
| ↑*Barnesiella* (3y) | ↑ Internalizing and externalizing behavior | NF | ↑*Barnesiella* in (constipated) ASD (S. Liu et al., 2019) (Zhao et al., 2019) | ↓*Barnesiella* in ASD (Averina et al., 2020) | GABA |
| ↑*Butyricicoccus* (1y) | ↓ Externalizing behavior | NF | ↑*Butyricicoccus* in constipated ASD vs non-constipated ASD (Dan et al., 2020) |  | Butyrate |
| ↑*Butyricicoccus* (3y) | ↑ Externalizing behavior | NF | ↓*Butyricicoccus* in ASD (S. Liu et al., 2019) |  |  |
| ↑*Streptococcus* (2w) | ↑ Externalizing behavior | NF | ↑*Streptococcus* ASD (Bundgaard-Nielsen et al., 2020); ↑*Streptococcus* in Bipolar disorder (Järbrink-Sehgal & Andreasson, 2020) |  | GABA and tryptophan |
|  | ↓ Executive functions | NF |  |  |  |
| ↑*Streptococcus* (12w) | ↓ Executive functions | NF |  |  |  |
| ↑*Clostridium* sensu stricto 1 (1y) | ↑ Externalizing behavior |  | ↑*Clostridium* in ASD (De Angelis et al., 2013; Kandeel et al., 2020) |  | Neurotoxins |
|  | ↓ Executive functions | ↑*Clostridium* at 2.5 months with attention (Aatsinki et al., 2020) |  |  |  |
| ↑*Intestinibacter* (12w) | ↑ Internalizing behavior | NF | ↑*Intestinibacter* bartlettii in children with neurodevelopmental disorders (Bojović et al., 2020) |  | Neurotoxins |
|  | ↓ Executive functions | NF |  |  |  |
| ↑*Bifidobacterium* (3y) | ↑ Internalizing behavior | NF | ↑*Bifidobacterium* in MDD patients (Knudsen et al., 2021) | ↓*Bifidobacterium* in ASD (Xu et al., 2019);  ↑*Bifidobacterium* less ASD symptoms (Grimaldi et al., 2017);  ↓*Bifidobacterium* in MDD patients (Cheung et al., 2019) | GABA, dopamine and noradrenaline |
|  | ↑ Externalizing behavior | NF | ↑*Bifidobacterium* in ADHD patients (Aarts et al., 2017) | ↑*Bifidobacterium* *longus* positive on ADHD (Finegold et al., 2010; Pärtty et al., 2015) |  |
| ↑*Blautia* (3y) | ↓ Internalizing behavior | NF | ↓*Blautia* in ASD patients (F. Liu et al., 2019) | ↑*Blautia* in MDD (Cheung et al., 2019) |  |
|  | ↑ Executive functions | NF |  | ↑*Blautia* with worse ADHD symptoms (Laue et al., 2021) |  |
| ↑*Halomonas* (6w) | ↑ Externalizing behavior | NF |  |  | GABA and tryptophan |
|  | ↓ Executive functions | NF | ↑*Halomonas* in Alzheimers (Wu et al., 2021) |  |  |
| ↑ *Bacteroides* (6w) | ↑ Inhibitory control | ↑ *Bacteroides* with better cognition at 2 years (Carlson et al., 2017; Tamana et al., 2021) |  |  | GABA |
| ↑ *Subdoligranulum* (1 y and 3y) | ↓ Inhibitory control | NF |  | ↓*Subdoligranulum* in patients with anxiety (Chen et al., 2019) |  |
| ↑ *Anaerostipes* (1 y) | ↓ Inhibitory control | NF | ↓ *Anaerostipes* in children with autism (Iglesias-Vásquez et al., 2022) |  | Butyrate |
| ↑ *Lachnospiraceae* NK4A136 (1y) | ↓ Inhibitory control | NF |  |  |  |
| ↑ *Ruminococcaceae* UCG-013 (1y) | ↑ Inhibitory control | NF |  |  |  |
| ↑*Sutterella* (1y) | ↓ Inhibitory control | ↑ *Sutterella* with better cognition at age three years (Rothenberg et al., 2021) | ↑ *Sutterella* in children with autism (L. Wang et al., 2013; B. L. Williams et al., 2012) |  |  |
| ↑ *Coprococcus* 3 (1y) | ↓ Inhibitory control | NF |  | ↑ *Coprococcus* 3 in healthy patients compared to patients with anxiety disorder (Chen et al., 2019) | Tryptophan |
| ↑ *Veillonella* (1y) | ↑ Inhibitory control | ↑ *Veillonella* with better cognition at five years (Guzzardi et al., 2022) |  |  | Immune system, interleukin pathways |
|  |  |  |  |  |  |
| ↑Alpha diversity (2w) | ↓Internalizing behavior | ↑alpha diversity with less internalizing behavior in boys Laue et al. (2021);  ↓Alpha diversity in children above the clinical threshold for internalizing behavior (van de Wouw et al., 2021) | ↓alpha diversity in ASD children (Kang et al., 2018; S. Liu et al., 2019; Ma et al., 2019) | No difference in alpha diversity between ASD  patients and healthy controls (Li et al., 2021) | GABA and norepinephrine |
|  | ↑Executive functions | ↑alpha diversity and worse cognition (Carlson et al. 2017) | ↓alpha diversity in ADHD (Prehn-Kristensen et al., 2018) | No differences in alpha diversity between ADHD patients and healthy controls (Hai yin Jiang et al., 2018; Richarte et al., 2021; Szopinska-Tokov et al., 2020; Wan et al., 2020). |  |
| Notes. NF, Not Found (i.e., no comparable findings in the literature for behavioral problems or executive functions). | | | | | |